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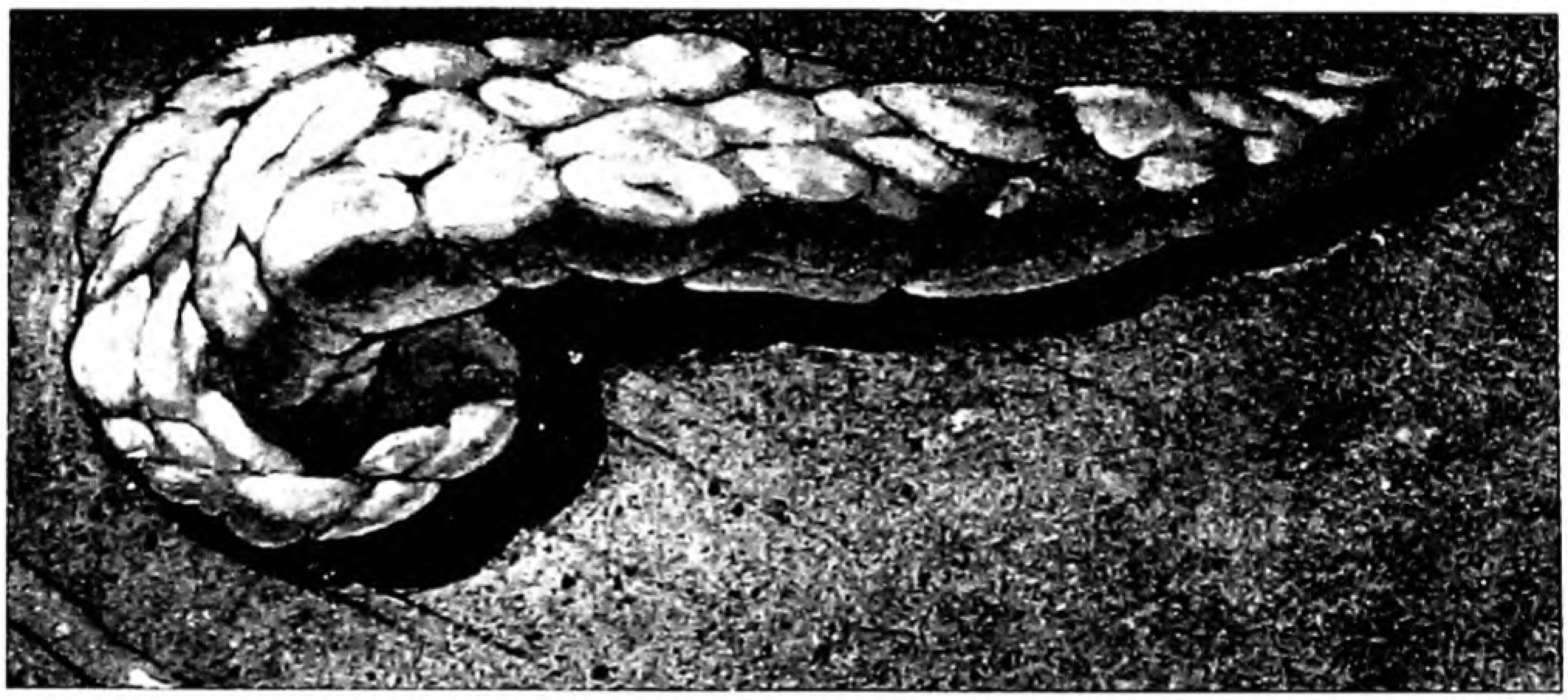

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EDITORIALS

Diabetes Mellitus (Type-2) Case for Postprandial Glycemic Control: A Paradigm Shift

Diabetes mellitus is perhaps one of the oldest diseases known to mankind, which has been catalogued in written record of many civilizations. It happens to be the most prevalent endocrine disease in the world today. It is estimated that by the year 2000, there will be 100 million people with diabetes worldwide. The prevalence of diabetes ranges from 2% to 5% in Europe, and it is estimated that there are 16 million people with diabetes in the United States; about half of these still remaining undiagnosed. About 90% of all diabetics belong to non-insulin dependent category (NIDDM or Tye-2 Diabetes Mellitus).

Diabetes has higher relevance in certain ethnic groups, and this underscores the need for epidemiologic stratification in order to target those at risk with approximately 50% of the population being affected. Hispanics, Asian Indians, and blacks tend to have 1.5-2 fold higher prevalence rates compared to caucasians. Undiagnosed type-2 diabetes is not a benign condition. About 60% of these patients have hypertension and roughly 50% have dyslipidemia. Hypertriglyceridemia may be seen in about a third of patients and more so if obesity is also present.[1]

Diabetes is an expensive disease. It extracts tremendous costs affecting both the patient and the society at large. In the United States treatment of 4.4% of its diabetic population amounts to $ 106 billion per year. This does not take into account human costs of loss of days at work, treatement of associated disabilities such as depression etc. The high cost of diabetes is related to the nature of disease which is insidious in onset and associated with micro and macrovascular disease, and neuropathy. Much of diabetic complications can be related to the burden of hyperglycemia. Studies done across continents show a direct-relationship between the level of glycosylated hemoglobin and macro or microvascular complications[2,3]. From experience gained in only few carefully designed intervention studies in type-2 diabetes patients, it appears that trends observed in Diabetes Control and Complications Trial (DCCT) in type-1 diabetes patients seem to hold up. It would appear that modalities that reduce hyperglycemia should help prevent complications in type-2 diabetes in the long term. The ongoing United Kingdom Prospective diabetes study (UKPDS) should provide some definitive answers. The results are expected in 1998.

Type-2 diabetes is a staged process that begins with genetic predisposition followed by insulin resistance and culminating in frank insulin deficiency. In the early stages postprandial hyperglycemia may be the only abnormality and, therefore, easily overlooked since fasting hyperglycemia has been taken as the hallmark of diabetes in general in the past. That post prandial hyperglycemia could be related to diabetic complications is only beginning to be appreciated. The classic Pima India study in Arizona revealed postprandial hyperglycemia to be clearly associated with retinopathy.[4] Over 6 year period 20% of subjects with postprandial blood glucose exceeding 200 mgs/dl developed retinopathy compared to 1% of subjects with lower postprandial glucose concentration. Retinopathy was observed in 9% of those with low fasting plasma glucose concentration but high postprandial glucose level. None developed retinopathy or nephropathy if the postprandial plasma glucose was less than 200 mgs/dl during a three year follow up. At 6 years of follow up retinopathy was noticed in only 3% and nephropathy (Proteinuria) in 1%. Postprandial hyperglycemia has been shown to be associated with increase in intimal plus medial wall thickness (IMT) of the carotid arteries of asymptomatic hyperglycemic patients without diabetes.[5] This association is independent of smoking, hyperlipidemia and hypertension.

With newer understanding about the significance of postprandial hyperglycemia vis-a-vis onset of vascular complications, goals of treatment have shifted. Previously therapeutic goals centered around symptom relief and normalization of fasting hyperglycemia. The new goal emphasizes normalization of postprandial hyperglycemia. This shift has been driven by the results of two intervention studies (Kumamoto study, and Hellman study)[6,7]. In kumamoto study 6 years of intensive insulin therapy that reduced average blood glucose from 220 to 150 mgs/dl significantly lowered the incidence and delayed the progression of retinopathy and nephropathy. Additionally there was protection against worsening of nerve function. In Hellman study done in the United States, intensive treatment in diabetic patients resulted in decrease in severe renal failure, cardiac specific mortality and total mortality. It is important to note that to prevent or delay sequelae of diabetes, early intervention is necessary. This creates a dilemma since the interval between the onset and diagnosis of type-2 diabetes may be as long as 10-12 years given the insidious onset and lack of dramatic symptoms.

Currently goals are defined by fasting, postprandial and bed time blood glucose levels as well as the level of glycosylated hemoglobin. The main planks of treatment are diet and exercise layered with addition of oral antihyperglycemic agents and/or insulin. However, none of these approaches directly tackle postprandial hyperglycemia.

A new approach to treating postprandial hyperglycemia needs to be adopted. Several possibilities exist. First a switch from traditional three meals to six small meals per day. This can reduce the caloric intake at a given time and reduce post prandial rise. Alternatively carbohydrate absorption and digestion may be delayed by use of alpha-glucosidase inhibitor, acarbose.[8] This drug is available in several countries and when taken with first bite of meal it reduces the postprandial glycemic excursion. It has no significant effects on lactase activity. Acarbose can be used in combination with sulfonylureas to treat diabetes. It must be pointed out that since acarbose prevents hydrolysis of sucrose to glucose and fructose, sucrose should not be used to treat hypoglycemia in patients taking acarbose. Another alternative would be to use insulin sensitizer (thiozolidinedione drugs such as Troglitazone) to reduce post prandial hyperglycemia. This class of drugs has a unique mode of action whereby they facilitate insulin signal transduction via interacting with gamma -PPAR receptor.[9] It is also possible to use insulin analog (Insulin Lys-Pro) which has rapid onset of action and hence becomes readily available to dispose glucose load. It has been shown to reduce postprandial hyperglycemia and protects against delayed hypoglycemia generally seen with standard regular insulin.[10] Although not specifically designed to blunt postprandial glucose excursions, oral sulfonylureas and biguanides when used judiciously will also lower postprandial blood glucose.

The possibility of manipulating postprandial hyperglycemia has given birth to new paradigm in type-2 diabetes management. A staged approach needs consideration. It would require understanding of pathobiology of disease on part of treating physicians and education of patients. Following strategy appears logical and worthy of trying.

- Dietary Intervention including limitation of caloric intake per meal (Introduce small fequent meal plan).
- Slowing down of carbohydrate absorption and digestion (Introduce Acarbose).
- Oral sulfonylureas: when above measures alone are not sufficient. Since these agents primarily act by releasing insulin, weight gain and hypoglycemia can occur.
- Add biguanide (Metformin) to reduce hepatic glucose output By itself it will not cause hypoglycemia. Furthermore it may cause some weight loss.
- Providing increase in insulin concentration immediately before and during meal only (introduce Insulin Lys-Pro). Insulin Kick.
- Enhance peripheral sensitivity to insulin (Introduce Troglitazone).

This stepped care approach should help vast majority of patients with type-2 diabetes mellitus. Where dyslipidemia and hypertension also coexist, they should be treated aggressively. Very soon many other antihyperglycemic agents will be made available including a new nonsulfonylurea oral agent that effectively reduces hyperglycemia.

Clearly we are poised on new dawn in type-2 diabetes management. It is incumbent upon all involved in the delivery of health care to take advantage of newer tools available if we are to change the course of this revaging malady.

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Primary PTCA for Mananging Acute MI-Current Status

The introduction of thrombolytic therapy in 1960's and 1970's represented a major breakthrough in the therapy of patients with acute myocardial infarction (MI). However within a decade of its widespread use a number of serious limitations & deficiencies of this form of treatment came to surface. These deficiencies include high rates of recurrent ischemia, reocclusion, catastrophic intracranial bleeding as well as the inability of these agents to restore normal flow in a large number of infarct related arteries. Percutaneous Transluminal Coronary Angioplasty (PTCA) undertaken as a "Primary" reperfusion strategy without prior thrombolytic therapy first reported in 1986 achieves rapid, complete reperfusion more effectively than thrombolytic therapy in several studies (1-8). Despite the availability of fibrin specific agents, front loading and adjunctive anticoagulation only 54% of patients treated with thrombolytics have complete reperfusion with TIMI 3 flow. With current experience, primary angioplasty can have a success rate of upto 97% with complete reperfusion and TIMI-3 flow established in approximately 93% of cases.

The mechanisms producing the improved clinical outcomes with primary PTCA are multifactorial. It is well established that normal flow (TIMI grade 3) is an important determinant of survival. After intravenous thrombolysis short term patency rates range from 54% to 81% of patients. Conversely higher rates of short term patency (95-99 percent) and normal flow (90-95 percent) are probably responsible for the improved prognosis with primary PTCA. Although it requires approximately 30 more minutes to initiate the PTCA procedure than to begin thrombolysis, reperfusion can be achieved quickly once the patient is in the laboratory and the mean time to reperfusion may actually be shorter with PTCA. Unlike thrombolysis, PTCA achieves a widely patent lumen with no clinically significant residual stenosis in more than 90 percent of patients.

Reocclusion increases the risk of reinfarction, death or congestive heart failure and prevents the recovery of ventricular function. After thrombolysis early reocclusion occurs in 5-10 percent of patients and late reocclusion in 30 percent. Thus combining 20-50% patients in whom reperfusion initially fails with the 30% patients who have late reocclusion, it is clear that long term patency may be expected in only 50% of patients after thrombolysis.[3,12] The rate of long term patency after primary PTCA is clearly superior to that with thrombolysis. An additional advantage of primary PTCA as seen from the pooled data is a very significant reduction in the rate of strokes(0.3 percent vs 2.5 percent p=0.007)[3,5,9]

A cumulative meta-analysis of all the trials comparing primary PTCA with fibrinolytics reveal that primary PTCA confers a small but significant reduction in the combined end point of death or non-fatal myocardial infarction and a trend towards improved survival.[3,9] Based on these data Primary PTCA should be the preferred strategy for acute MI when both options are available. Recent advances in adjunctive therapies to PTCA including platelet glycoprotein IIb/IIIa antagonists and newer technologies like stents may further extend the benefits of angioplasty over fibrinolytics.

Intra coronary stents have dramatically changed the therapy of failed angioplasty and acute vessel closure. Stents have also conferred a significant restenosis benefit.[12,13] The presence of intra coronary thrombus during plaque rupture was first considered to contraindicate the use of coronary stents. However recent reports have shown that adequate stent deployment in presence of a thrombus and in acute MI states have shown a favourable clinical outcome.[14,15] In hospital reocclusion and mortality rates for bail out stenting in primary PTCA were very low in the study of Rodriguez et al.[15] These favourable results have made primary stenting as an alternative reperfusion strategy. In a recent study Saito et al[16] have shown primary stenting when compared with matched controls who underwent direct PTCA during the same period dramatically reduced the major clinical events (18% vs 3%) and restenosis rates (41% vs 17%). A number of prospective randomised studies to address this issue are underway.

Mechanical reperfusion therapy of acute MI continues to evolve rapidly. The use of stenting for failed angioplasty, the advent of new antiplatlet regimens and new thrombectomy devices all show promise to further improve the rate of sustained arterial patency after acute MI. It is realistic to anticipate that patients undergoing mechanical reperfusion therapy will have more than 95% rate of TIMI-3 flow, less than 1% rate of reocclusion and mortality rates as low as 2%. However to compare contemporary primary PTCA with fibrinolytics, a large prospective randomised trial would have to include the use of primary stenting with angioplasty and glycoprotein IIb/IIIa inhibitors with both strategies. The relentless pursuit to open an infarct related artery promptly with sustained patency and efficacy thus continues and we were fortunate to have extremely attractive approaches to alter the natural history of a once lethal disease.

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The Burden of Landmines

The signing of the treaty at Ottawa, Canada, to ban anti-personnel landmines by 125 countries in the first week of december 1997 is appropriately signalled as "a historic victory for the weak and the vulnerable of the world, "by the leader of the United Nations. The victory may not be complete as many countries including the United States, Russia, China, Turkey, Iran, Libya, India, Pakistan, Egypt, Isreal, North Korea, South Korea and Vietnam holding out at present, but not completely ignoring the call.

Mines may be described as fighters that never miss, strike blindly, donot carry weapons openly and go on killing long after hostilities have ended. In short, mines are the greatest violators of International humanitarian law, they are the most ruthless of terrorists. Every year, in numerous war-torn countries, thousands of men, women and children are victims of mines. Some mines are simple devices, while others make use of advanced technology. But all of them kill and cause severe mutilation. Every month 60 people on an average are killed or injured by them. Between 1945-1977, about 15 million mines were cleared from Poland. In the same period, some 4000 civilians were killed and 9000 injured by mines. There are an estimated 100 million mines scattered round the world. These mines in addition to killing, maiming and terrorizing, have the power to deny by their very presence the fundamental right of refugees to return to their native lands.

Judy Williams - The Crusader

In Angola, after 15 years of war there are an estimated 20,0000 amputies, all victims of mine blasts. The majority are women and children. In some countries farmland can not be cultivated because it is strewn with mines, a situation that during the war gave rise to chronic malnutrition. For certain population groups the inability to cultivate their land is a threat to their very survival, also cause damage to natural environment. International humantarian law affords protection for environment, to safeguard the health and survival of the population. The problem in our state of Kashmir may not be as grave, nonetheless `modified landmines' are taking their toll. In trouble-torn state of J&K, a survey conducted by `JK Yateem Trust' revealed that there are over 15,000 orphans, 6,500 disabled and 12,000 widows in Kashmir Valley and this speaks of impact of violence in the past 9 years, but the contribution of the landmines in the countries like India, Pakistan and China is not accurately available. In Afghanistan a manually launched mine clearance programme would take 4300 years to make 20% of the country free of mines (at the rate of clearing 30 sq.m per year). In Combodia it is estimated that 4 million to 6 million have been buried by the rival armies.

Mines produce damage by either blast or penetration of metallic fragments. Those tigerred by foot pressure wound by blast. The tissues of the foot are exploded or legs are simply blown off. Damage is rarely confined to one leg, lesser but severe damage is frequently caused to other leg, the genitals, arm, chest and face. With the explosion dirt, mud and other debris is driven into the tissues. Individuals within the lethal radius die from blast and fragmentation, injuries to those more peripheral to the explosion are by metallic fragments or spheres, stakes and directional mines cause similar injury to those outside the lethal radius.

Surgeons recognise three patterns of injury produced by mines. Traumatic amputation of the part of the lower limb and less severe injuries elsewhere, multiple fragment wounds on the upper limb, chest and face damage caused by handling. These cases are particularly problematical because injuries of this severity and the degree of contamination are rarely seen in civilian practice and few surgeons have experience and skill in dealing with such wounds.

ICRC was the first to introduce the concept of mine awareness into its first aid courses in Pakistan. Some 20,000 victims were treated by ICRC surgeons in 1991. ICRC orthopedic workshops in 14 countries made limbs for 7876 amputees and produced 11, 116 orthopedic appliances in 1991. For the varied and extensive injury to the body, a multidisciplinary team is needed to treat landmine victims on emergency basis in fully equipped trauma units in major hospitals and towns. Our medical college in the heart of the city and the Medical Institute at Soura in Kashmir have developed sucha unit on a small scale, but needs more expansion and modernization in staff and equipment.

Fortunately the international compaign to ban landmines started in 1992 and backed by about 1000 non-governmental organisation (NGOS). The International Committee of the Red Cross (ICRC), the Red Crescent Societies and others were able to focus the world opinion in favour of a ban on the use of landmines. With celebrities like princess Daina throwing her bit, the campaign gained accelerated momentum. Judy Williams the American co-ordinator of this International Compaign against landmines shared the Nobel peace prize for the year 1997 which was awarded to her on 10th August 1997. The efforts of the campaign culminated this December (1997) in signing of a treaty at Ottawa. The treaty requires the signatories to destroy their stockpile of mines within four years and remove deployed mines with ten years.

We have still a long way to go before we make the world safer for children like Song Kosal-a 13 years old girl who spoke as member of the Combodian delegation at Ottawa having lost her leg at the age of 8 to a landmine when she was herding animals in her village. The world should take note and act without delay to reach the goal which Jean Chretein the Canadian prime minister - the first country to sign the treaty - has set, "THE SLAUGHTER MUST END"

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Hepatocellular Carcinoma in Paediatric Population

Hepatocellular carcinoma (HCC) is a relatively rare tumor in young individuals. HCC constitutes 0.7% of malignant hepatic tumors in children[1]/or paediatric populations. HCC has a median age and onset of 12 years. The age range is wide however and may be influenced by associated underlying disease. The mean age of presentation in fibrolamellar subgroup is 20 years with few cases seen before age of 10 years[2]. HCC in children younger than 15 years shares strong association with hepatitis B virus. Clear cases have been documented of perinatal transmission of HBSAg, with development of HCC 6 to 7 years later[3]. The causative role of hepatitis C virus was first suspected in Japan. Hepatitis C related HCC effects older patients and underlying cirrhosis is more advanced and tends to be small and expanding in growth pattern[4]. Children with chronic form of hereditary tyrosinemia who survive beyond age of 2 years have a striking high incidence of HCC[5]. Children with homozygous ZZ phenotype alpha-anti-trypsim deficiency are associated with high incidence of HCC and cholangiocarcinoma[6]. Glucose 6-phosphate deficiency (type I glycogen storage disease) has been associated with liver disease which are benign however, reports of HCC developing in longer-time survival exists[7]. HCC has been reported in children with lymphoblastic leukemia treated with daily oral methotrexate[8] other associations of HCC include neurofibromatosis[9], ataxia telangiectasia and familial adenomatous polyposis[10].

Pathology

HCC is childhood is similiar in gross and microscopic features to its adult counterpart except for the lack of underlying cirrhosis. A distinctive variant of HCC occurs in non-cirrhotic livers of older children and young adults. This tumor, termed fibrolamellar carcinoma has a more favourable prognosis[2]. Other procedures that help prove the diagnosis are demonstraction of Alpha feto protein (AFP) and alpha-anti trypsin by light or electro immunohistochemistry.

Presenting Features

In a report of 71 pediatric patients by Yen Hsuan NI[11] the main presenting feature was abdominal mass (10.8%) abdominal pain (38.1%), anorexia (12.7%), malaise (9.9%) and fever (7%) only 1.4% had jaundice, and purpura. Main physical finding was hepatomegaly (97%) splenomegaly (42%), ascites 25%, jaundice in 23% and internal bleeding in 4%, .26% children had features of cirrhosis.

In adults symptoms mainly caused by cirrhosis, such as ascites, pedal odema and jaundice are more common (80-90%). In a series of 2520 cases from a report of the Japan Cancer study group, general malaise occured in 59.4% patients with HCC, abdominal pain 45.3%, weight loss, ascites and palpable mass in 25.7%, 22.7% and 21.7% of patients with HCC respectively, while jaundice occured in only 14.7%, high fever occured in 14.7% and is often associated with poorly differentiated HCC.Smaller HCC are more frequently detected in recent years by improved imaging techniques and regular check up of liver disease usually not associated with any symptoms caused by tumor[12].

A number of studies in adults have shown that cirrhosis is a major predisposing factor in development of HCC. A similar etiopathogenic relationship exists with viral hepatitis B and carrier, have 22 fold risk of developing HCC because of role of B viral infection in oncogensis since viral DNA has been found to be integrated into host genome of both HCC and non-tumour like liver tissue[13].

Diagnostic Workup

Mild normocytic anemia is usual although polycythemia is occasionally seen. Modest elevation of liver enzymes and alkaline phosphates can occur. Bilirubin is infrequently elevated. Most valuable laboratory test for both diagnosis and monitoring of hepatic tumor is (AFP). This fetal protein is a single chain dilated glycoprotein with mol. weight of 67,5000 dlatons. It's synthesis begins at 28 days of fetal life by liver. By 14 weeks peak levels are reached and there after a rapid decline occurs until term. At 1 years, adult levels of 3-15 ngm/ml are reached. Levels are elevated in upto 50% of childhood HCC[14]. Other investigation include exposure to HBV and òHCG (human chronic gonadotrophic hormone) level in children with precocious puberty[15].

Diagnostic Imaging

Chest films may demonstrate elevation of the right hemidiaphram. Hepatomegaly may be discerned on plain abdominal films and displaced duodenal gas is an indirect sign of hepatomegaly. Radionuclide imaging using technetium 99m labelled sulphur colloid although very sensitive technique has low specificity. Even with single photon emisson computed tomography (SPET) or positron CT, the sensitivity is still inferior to ultrasonography or CT scan. Only half of hepatic lesions about 2 cm in size are visualized by (SPET)[16]. For these reasons; radionuclide scanning is much less frequently carried out for diagnosis of hepatic tumor.

Ultrasonography : Ultrasound using linear convex sector transducer is a useful and practical method for detecting focal lesion within the liver. Diffuse liver disease particularly liver cirrhosis is also diagnosed by ultrasonography by irregular surface fo liver, splenomegaly, dilated portal and gastric veins and ascites. Distinction of large HCC and metastatic cancer by echo pattern alone may be difficult but the latter is more often multiple. Small HCC's are usually distinguished from a metastatic lesion because they are typically hypoechoic while metastatic lesin are isoechoic or hyperechoic[17]. An important merit of ultrasonography is its capability of demonstrating major portal and hepatic veins and intravascular tumour invasion.

Computed tomography (CT) : Neoplastic lesions in the liver usually are seen as areas of decreased attunation, but occasionally they are isodense or hyperdense because of calcification. The reported accuracy of CT for metastic liver tumors has been around 90% and for HCC, it is about the same. Main features that assist in diagnosis of HCC from metastatic cancer is suggested by presence of an isodense mass, a narrow circular zone surrounding the mass (capsule), bulging of the tumor from the liver surface and presence of cirrhotic changes[18].

Lipiodol computed tomography : In this technique several milliters of lipiodol, an iodized oil contrast medium is injected into hepatic artery and CT scan performed 10 days to 2 weeks later. Lipiodol remains in tumor for long period. A lesion as small as 3mm may be discerned. Lipiodol CT is perhaps the most sensitive of all imaging modalities for diagnosis of small but overt HCC[19].

Magnetic resonance imaging (MRI) : The diagnostic accuracy of MRI is about the same as CT but MRI provides information about blood flow and tissue diagnosis. The capsule around HCC is clearly seen as a low intensity circle around it. On T_1 weighted images and together with mosaic interior, it constitutes characteristics feature of HCC[20].

Treatment

Prognosis of patients with HCC is generally poor and largely depends on size of tumor, growth speed, the degree of cirrhotic changes and underlying disease. Treatment of children with malignant liver tumor has been unsuccessful apart from surgical resection. Complete removal of primary lesion still offers the best chance of survival. A recent survey in Japan demonstrated that 1306 patients who had curative hepatic resection (with a sufficient clean margins) had a median survival of 3.6 years and 7 years survival rate of 46%[21]. Radiation therapy has been ineffective in controlling all but localized tumor in the liver possibly because an effective antitumor dose is above liver tolerance[22]. Combination chemotherapy (Vincristine, Adriaymcin, cyclophosphamide, and 5-fluorouracil) have been tried in children with HCC in 6 weekly cycle for 1 year. Surgical resection and irradiation were employed when indicated. Patients were followed for 12 months. 24 patients had no measurable disease following surgical treatment and chemotherapy at median 30 months. In 27 patients with residual measurable disease response rate was 44% lasting median 18 months[23], percutaneous ethnol injection therapy (PEIT) has been used in HCC. In a study by Shuichiro Shiiha[24] used PEIT in 18 patients along with transcatheter arterial embolisation in 10 patients. On repeat histopathological examination noviable tumor was found in 3 of 18 tumours and all showed coagulation necrosis. In PEIT absolute ethanol destroys the tumor tissue directly and immediately through its non-selective desaturation effect on cellular proteins. In other five cases in which some portion of tumor was not destroyed, the viable tumor was left in small nodules around main tumor. The survival rates of patients undergoing liver transplantation and resection for HCC stage III and IV have been similar and poor with about 20% survival after 2 years[25].

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REVIEW ARTICLES

Management of Head and Neck Cancer

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Introduction

Head and Neck cancer include a heterogeneous group of cancers involving lip, oral cavity, oropharynx, hypopharynx, larynx, nose and paranasal sinuses and nasopharynx. Major advances have been made in the diagnosis as well as treatment modalities of head and neck cancer which includes organ preservation, chemoprevention and the use of newer tools like cryoapparatus and laser beam.

In this review, the diagnosis of and standard therapy for head and neck cancer as well as the status of newer diagnostic and therapeutic technique is discussed. The salivary gland, thyroid, ocular, brain, skin, parapharyngeal and the rare tumours of other histologic types (lymphoma) are not included in the discussion.

Aetiopathogenesis

Approximately 9% of all human cancers involve the head and neck region. Roughly 42,800 cases of head and neck cancer are estimated to have occurred in the United States with 11,600 deaths during 1992. Worldwide, more than 500,000 new cases are projected annually.[1,2] In India the upper aerodigestive tract cancer, which include the oral cavity, oropharynx, hypopharynx and oesophagus constitutes nearly 30-35% of all cancers seen in the body.[3,4] The male to female ratio is 4:1 but the number of females affected is on the increase. Majority of the head and neck cancers are squamous cell carcinoma.

Alcohol and cigarette smoking constitute the most important risk factors[5,6]. Alcohol, besides being an independent risk factor also potentiate tobacco-related carcinogenesis. Occupational risk factors include exposure to nickel and textile fibers and woodworking.[5] In our country oral malignancy is one of the most common malignancy due to the widespread habit of chewing tobacco and betel nut. Also there is increasing incidence of buccal mucosa carcinoma seen in people from eastern region because of their habit of keeping tobacco and lime in the mouth. The role of asbestos exposure in case of laryngeal cancer is still controversial. Dietary factors may also play a part in Head and Neck malignancy. There is a inverse relationship between the consumption of fruits and vegetables and the incidence of head and neck cancer,[8] although the specific protective components of these foods remains to be identified.

Viruses have also been thought to be contributing factor in Head and Neck malignancy. DNA from human papilloma virus has been detected in cancerous tissue from the Head and Neck[9] and Epstein-Barr virus is associated with nasopharyngeal carcinoma.[10] Genetic predisposition to Head and Neck malignancy is also suggested due to its sporadic occurrence in young adults, non smokers and non-alcoholics.[11] Mutagen-induced chromosomal fragility in cases of head and neck malignancy has been implicated as a possible risk factor in the development of second primary tumor.[12]

Diagnosis and Staging

Majority of the head and neck malignancy occurs in males in the fifth decade or later. The signs and symptoms depend upon the primary lesion as well as the stage of the disease. In the early stage, patients usually have vague symptoms and minimal findings, however, advanced malignancy is easily diagnosed due to presence of tell-tale signs and symptoms. For diagnosis of early lesions, it is therefore mandatory that one must have a high index of suspicion, particularly if the patients uses tobacco and alcohol.

For diagnosis of various Head and Neck malignancy it is essential to take a detailed history followed by

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thorough clinical examination particularly with reference to the area of involvement. The patient is then subjected to a battery of investigations including C.T. scan and MRI. C.T. scan helps in not only knowning the extent of the lesion but also in the staging of the disease. Final confirmation of the disease is made on the basis of histopathological examination of biopsy material or FNAC.

Lip and Oral Cavity

Malignancy of the lip usually involves the vermilion border and mucosal surfaces. Lower lip is affected in 90% of the cases and roughly 95% of the cases and roughly 95% of cases are squmous cell carcinoma. Neck node metastasis is seen in 5% of lip malignancy is detected early, it is equally cured by radiotherapy or by surgery and the choice lies with patients comfort and convenience.

In T-is and T_1 lesions (<= 1cm) are treated with radiotherapy or surgery. In T_{1-4} lesions (> 1cm) radiotherapy and surgical excision give similar curative results but radiotherapy is preferred, where commissure is involved since it is cosmetically and functionally better than surgical excision. Local tumour control is achieved in more than 90% cases where lesion in <3cms and it is 75%-80% for larger lesions. Neck nodes, if present, should be treated as per any situation.

Malignancy of the oral cavity involves floor of the mouth, tongue, buccal mucosa, hard palate and retromolar trigone. In these cases the choice between surgery and radiotherapy depend on the anticipated functional result, patients status and the need for treating nodal metastases. Early lesions ($T_{1,2}$) of the floor or mouth or tongue may be excised trans-orally, if adequate safe margin can be obtained. For larger midline lesion, mandibulotomy may have to be performed, where as lesions of the lateral floor of the mouth are treated with a partial mandibulectomy and neck dissection. T_1, T_2 tongue lesions are treated with partial glossectomy. For gingivia and hard palate early lesions are treated with surgery and advanced lesions by surgery and radiotherapy. Small tumours are usually locally controlled and in T_4 lesions local control is seen. Incase of buccal mucosa cancer, T_1 lesions are treated with surgery or radiotherapy, $T_{2,3}$ lesions are treated with radiotherapy. T_4 lesions are treated with a combination of surgery and radiotherapy. 90% tumour control is seen in T_1, both radiotherapy and surgical excision are associated with 80-90% and 50-80% survival rates for stage I and stage II tumors respectively.[13]

Approximately 35% of patients with tongue cancer present with clinically positive node. As primary lesion approaches or crosses the midline, there is risk of involvement of neck nodes on both sides. Patients having ipsilateral lymphnodes, run a 30% risk of metastases to the opposite side.[14]

Oropharynx

This includes anterior pillar, faucial arch, tonsillar fossa, soft palate, base of tongue (including vallecula), pharyngeal wall lesions. In T_1 and T_2 lesions of region, radiotherapy achieves more than 80% local tumour control.[14] Equivalent rates of local control is achieved with transoral excision and composite resection with a three to five year survival rates exceeding 60%[15]. For larger T_1 and T_2 lesions radiational disability and disfigurement which usually follow composite resection. Advanced lesions are treated with surgery and radiotherapy. In T_3 or T_4 lesions the five year survival rate is about 20%.

40-50% of patients of soft plate have cervical node metastases at the time of presentation. Small lesions are treated with radiotherapy. For large lesions resection can result in difficulty in speech and swallowing. 80-90% local tumour control is seen in T_{1-2} lesions and 75-80% local tumour control is seen in T_{3-4} lesions.

T_1 and T_2 lesions of the base of the tongue are usually treated with surgical resection with or without mandibular osteotomy and neck dissection. Composite resection is employed in lesions that are more than 2 cm. Local tumour control is seen in 70-80% of the cases[16]. Radiotherapy with or without brachy-therapy achieves 88-100% local control in T_1 lesions and 69-84% for T_2 tumours.[17] Prognosis of the base of tongue tumour is poor since most of these lesions are diagnosed at advanced stage.

In early pharyngeal wall tumour, radiotherapy is employed and in advanced lesions combined radiotherapy and surgery is employed. Local control is achieved in 30-50% of T_2- T_3 lesions. T_1 lesions in this region are rare.

Hypopharynx

Early exophytic lesions particularly in upper pyriform sinus is treated with radiotherapy. Other early T_1 and T_2 lesions are treated with total or partial laryngectomy with partial or total pharyngectomy or radiotherapy or combination of both. T_3 and T_4 lesions are treated with total laryngopharyngectomy and radiotherapy. In cases which are in-operable due to involvement of the posterior pharyngeal wall or massive neck involvement the treatment of choice is radiotherapy. The five year survival rate for T_1 and T_2 tumours is 60%. Most of these patients present with advanced nodal stage disease and the prognosis is poor.

Larynx

Radiation therapy is the commonly accepted treatment for early stage cancer of the vocal cords with survival rate of 96-98% in T_1 lesions and 80-90% for T_2 lesions. Endoscopic laser surgery or cryosurgery is an alternative treatment. Careful followup is required following these treatment modalities. For T_3 lesions either surgical excision (Total laryngectomy) or radiation therapy is employed. In cases with T_4 lesions of the vocal cords the treatment is total laryngectomy followed by radiotherapy. Local tumour control of 60% in seen in T_3 lesions and it falls to 30% if there is cervical metastases.

In T_1 supraglottic lesions either supraglottic laryngectomy or radiation therapy is employed. For T_{2-3} exophytic supraglottic cancer radiotherapy achieves good tumour control. Surgery is preferred for infiltrative lesions involving the base of the epiglottis or false cords. The lesions are treated by a combination of surgery and radiotherapy. Local tumour control is seen in 90-95% T_{1-2} cancers, 80% in T_3 cancer and 40-50% in T_4 cancer.

Early subglottic cancer is treated with total larygectomy or radiotherapy. Advanced lesions are treated by total laryngectomy followed by radiation therapy. Approximate 5-year survival rate is 30-40%.

Nasopharyx

Nodal metastasis is present in approximately 60-90% of patients with nasopharyngeal cancer. Lymphoepithelioma has a more favourable prognosis than squamous cell carcinoma. Radiation therapy alone is used for treatment of both the primary tumour and regional nodal metastases. Neck dissection is reserved for adenopathy that persists or recurs after radiation therapy in patients with apparently controlled primary sites. The five year survival rates range from 37-62% and influenced by the stage of the tumour and the percentage of patients with lymphoepithelioma.[18] Since the nasopharyngeal cancer particularly those with an advanced nodal disease, has a higher rate of systemic involvement, the use of chemotherapy is under investigation.[19]

Nose and Paranasal Sinuses

Early nasal cavity lesions are preferably treated with radiation therapy if surgery will produce a deformity. Surgery is preferred if bone is destroyed, if the lesion is a melanoma or sarcoma. For advanced lesions combined surgical resection and radiotherapy is the commonly used modality of treatment. Adjuvant chemotherapy is used for various types of sarcoma. Early nasal vestibule carcinoma are treated with radiotherapy or cryosurgery or lasar therapy. Advanced lesions are treated with radiotherapy alone. Local tumour control is more than 90% in small tumours. Recurrent or persistent disease after radiotherapy are treated with surgical, cryosurgical or laser excision. For ethmoidal sinus cancer combination of surgical and radiotherapy is employed with 30% five year survival rate. In cases with frontal and sphenoidal sinus cancer radiotherapy alone is used and results are dismal. Early maxillary antrum lesions are treated by surgery alone. In cases with advanced lesions surgical excision with either pre-or postoperative radiation therapy is the treatment of choice. In very advanced lesions initial chemotherapy followed by surgical excision and radiation therapy is employed. In unresectable lesions chemotherapy and high dose radiation therapy has been employed. Overall five year survival rate is 30% with 60% in patients with $T_{1,2}$ lesions.

Management of Cervical Lymphondes

There has been a lot of debate whether elective neck dissection for potential microscopic disease improves surival rate among patients having T_4 lesions with no clinically apparent neck nodes. It has been observed that both radiation therapy and neck dissection are seemingly equally effective in eradicating subclinical disease. Management of these neck nodes depends on the management of the primary tumour. If treatment of the primary is surgical then an elective neck dissection is frequently performed with 90% control of subclinical disease. Conservative neck dissection for NO, N1 cases with improved aesthetic outcome.[20]

Management of clinically positive cervical lymphnodes (stage N1-3) also depends on the management of the primary. When primary is treated by surgery, a neck dissection is sufficient for small nodal metastases (N1). Postoperative radiation therapy is added for N2 or N3 nodes and this will increase local control in the neck postoperatively as well as control subclinical disease on the opposite side of the neck.[21] Patients with nodal involvement from an unknown primary cancer may be treated with surgery or radiotherapy or both depending on the size and location of the node.

Chemotherapy

The single commonly accepted indication for chemotherapy is metastases or recurrent disease,. Various single agents have been tried in the past with poor results. Combination therapy particularly cisplatin and fluorouracil has resulted in better response with overall response rate of 11-79% and complete response of 0-27%.[22]

Local or Regionally Advanced Disease

Combined therapy like Induction and Adjuvant Chemotherapy have been tried in conjunction with surgical excision or radiation therapy. The overall response rate seen with induction chemotherapy has been more than 80% with complete response seen in 60% of the cases. However as the various trials have not shown increased survival rates with either induction or adjuvant chemotherapy,[23] the role of induction chemotherapy still remains investigational.

Organ Preservation

Since the organs in the head and neck region play a vital role in the normal daily function, efforts to conserve their presence and function without compromising complete tumour eradication must take a high priority in clinical research. In spite of continuous refinement of surgical techniques which has resulted in decreased mortality, the addition of chemotherapy to the treatment plan allow a further decrease in the need for radical surgical intervention. Various pilot trials using induction chemoutherapy[24] have revealed that surgery could be omitted without compromising survival in patients who responded to chemotherapy. In a large randomized trial of laryngeal cancer, where induction chemotherapy. In a large randomized trial of laryngeal cancer, where induction chemotherapy followed by radiation therapy was employed, preservation of larynx was feasible in 64% of cases. The survival rates in these cases was however not significantly different from those who were treated with laryngectomy and radiation. Organ preservation for head and neck cancer is still under investigation.

Cryosurgery and Head and Neck Cancer

Cryosurgery has been employed both as a primary treatment modality as well as adjuvant in cases with recurrence or primary lesion. It has also been employed for palliation of symptoms in incurable cancer. In a study where 50 patients with carcinoma of the oral cavity were treated with cryosurgery, local control of carcinomas was achieved in 90% cases for more than 2 years.[25] In another study where 80% patients with tongue carcinoma were treated with cryosurgery the survival rate of 5 years was 75%.[26] Cryosurgery has also been used in combination with chemotherapy and radiotherapy in stage III and IV carcinoma of the nasopharynx and a survival rate of 80% has been observed at 2 year interval.[27] In carcinoma of the maxillary sinus cryosurgery has been combined with radiation therapy and chemotherapy and it has been observed that the survival rate increased in these cases with avoidance of facial disfigurment.[28]

Chemoprevention

It has been observed that although early stage head and neck cancer can be succesfully treated with surgery or radiotherpy 3-7% cases annually develop second primary cancer. To prevent second primary cancer, strategies like chemoprevention i.e. administration of drugs to suppress carcinogenesis and prevent the development of second cancer has been tried. The ability of synthetic and natural retinoids to reverse leukoplakia have been studied extensively and response rates ranging from 55-100% have been observed.[29] In a trial where high dose of isotretinoin was given for three months followed by maintenance therapy with low dose of isotretinoin or beta-carotene, it was found that there was lower rate of progression of leukoplakia with maintenance therapy consisting of isotretinoin than beta-Carotene.[30]. Patients receiving high dose of isotretinoin as adjuvant therapy after surgery and radiation therapy were found to have a significant overall reduction in second cancer after treatment.[31]

The various clinical investigations during the past decade have led to several insights. Induction chemotherapy particularly those which include biological modulators, have shown to result in high response rate, reduced incidence of metastases and organ preservation. Improved local and regional control have also been observed with concomitant chemotherapy and radiation therapy. Cryosurgery and Laser surgery have a promising role in early lesions and are definitely superior to surgical knife particularly in patients who are elderly and belong to high surgical risk group. However there is still a need to strive for further improvement in the actual clinical end points-survival rates and the quality of life. Chemoprevention strategies have shown to reverse premalignant lesions and prevented development of second primary cancer. Its role need to be further expanded. With the increasing knowledge of tumour biology it may be possible for us in future to identify improvement prognostic factors and thereby formulate new treatment plan for head and neck cancer.

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ORIGINAL ARTICALS

The Importance of Prophylactic Closed Suction Drainage in Wound Care

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***Abstract** : Most dreaded complication in Orthopaedic wounds is infection which could be catastrophic especially in the presence of a metal implant. Early published evidence shows that drains are one of the potential risk factors for wound infection. It has given them the label which, in fact, they do not deserve, because there is a firm scientific basis for their widespread use in routine Orthopaedic surgery. Since wound healing and infection in operative wounds pivot around the haematoma formation, a retrospective study of the use of closed suction drainage in 340 Orthopaedic wounds revealed that the primary wound closure over a closed suction drainage system was proven to be a satisfactory practice. So it is advocated to be followed routinely in Orthopaedic Surgery where large blood collection is anticipated, as it seems reasonable that it is the most method of evacuating haematoma/seroma from a wound. Thus, providing a suitable environment for the wound healing and contributes to improving overall results, shortens the morbidity, and reduces hospital stay.*

***Key words**: Suction Drain, Wound haematoma, Healing infection, Orthopaedic surgery.*

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Introduction

The use of drains in Orthopaedic Surgery is as old as the subject itself. Although the type and material of the drain has revolutionized from simple corrugated rubber to the latest perforated plastic tube with suction.

Haematoma can develop in wounds in which adequate haemostasis has not been obtained, wounds in which dead space exists and in wounds involving medullary bone. Since haematoma is a potential culture medium for bacterial proliferation, in evacuation is essential for providing a suitable environment for satisfactory wound healing and to minimize morbidity, and financial burden which will otherwise follow wound sepsis. Closed suction drain has been a great advance for the evacuatiuon of blood and fluid from dead spaces, thus, allowing the adjacent tissues to resume their relationship to each other. At present, clinical assessment of each wound remains the only significant subjective method of measurement of wound healing.

A clinically significant infection of the wound can occur in presence of a foreign body or a prosthesis. But, when drain is inserted, this risk is increased. A closed suction drainage system is less risky and advantageous over an open separate 'stab' drain[1]. Suction drainage is routinely used in prestigious Orthopaedic institutions like Campbell clinics and A.O. centres with encouraging results. It has been reported from the Campbell clinics that they have had no infection in Arthroplasty of the hip when this type of drain was used[2].

In contrast to the reports favouring the use of closed suction drainage, Cobb[3] observed in a comparative study of 70 patients, who had an operation for fractured neck of femur, that drains increase the risk of infection, and no firm evidence that they aid wound healing.

To our knowledge little has been described in the literature and standard test books about the efficacy of suction drains eversince Waugh and Stinchfield[4] reported first on their use in Orthopaedic Surgery 30 years ago. Moreover, various published studies on the use of these drains have been directed towards their use in Arthroplasty of the hip and the knee, and the number of patients in those studies has also not been big[5,6]. So we assessed the role of closed suction drains in routine Orthopaedic Surgery.

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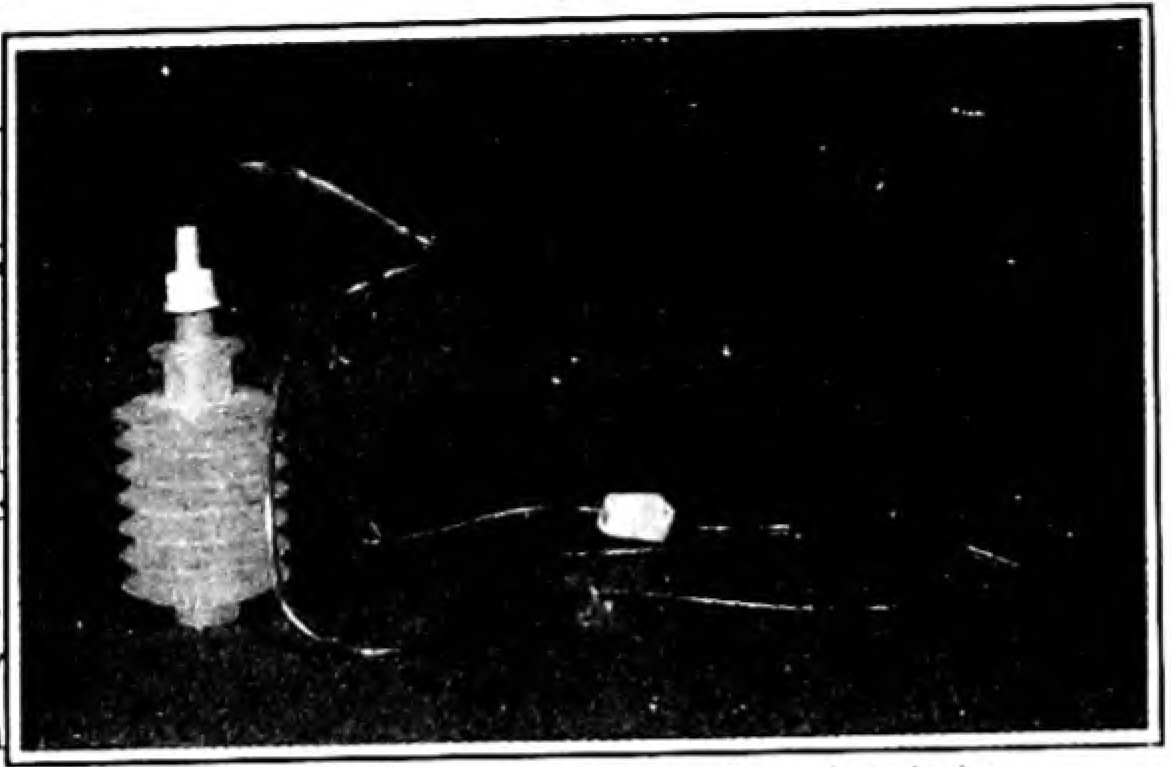
Material and Method

340 patients with fractures or other Orthopaedic pathologies were included in this retrospectie study. Patients' age, sex, diagnosis, date of admission, associated illness and date and type of operation were recorded. Patients were assessed and made fit for spinal'general anaesthesia. Pre and post operative blood transfusion was given in some patients depending on their haemoglobin levels.


Suction drainage set with needle redon drain

Patients had their wounds closed over one or two suction drains, dependig upon the site of operation and field of dissection, after proper haemostasis by electrocoagulation. Suction drainage set used consisted of a 'single use needle' redon drain (Perforated tube), and a connecting tube with a slide clamp attached to 400 ml. bellows. At operation, two drains were used for wounds around the shoulder, arm, forearm, hip, thigh and leg. One drain (perforated Portion) with an internal diameter of 4-6 mm. was placed close to the operation site of bone or metal implant (site of haematoma or seroma formation), and the other drain with internal diameter of 3 mm. in the subcutaneous fat (Group A). Single drain with internal diameter of 32 mm. was used as an intraoperative procedure for wounds around the elbow, knee, ankle, and foot (Group B). In both groups A & B, to avoid transmission of skin organism, non-perforated portion of the drains was brought out through a small separate skin incision with the help of needle attached to it. The main wound and the exit site of the tube were dressed separately as well, which allowed the removal of the drain without touching the main wound. The bellows was fully compressed while keeping the clamp open, then the tubing was reclamped and firmly attached to the redon drain through a rubber interconnector. Reopening of the clamp permitted the drainage of the wound haematoma by suction. The drains in group A were labeled as superficial (S) and deep (D). When bellows was filled to its capacity, it was replaced by another compressed bellows after clamping the tubing. In all cases the drains were removed at bedside at 48 hours using sterile technique, and the amount of fluid was measured. About 3 cm. of the tubing from its tip was put in a sterile specimen container and then sent for bacteriological examination. In group A tips from two drains were put in a separate containers labeled "S" and "D". Early mobilization of patients was employed from first postoperative day, progressing from bed exercises to sitting in a chair followed by walking without or with support (crutches or walking frame) as deemed fit for a particular case. On the seventh postoperative day each of the wounds was observed for redness, heat, swelling of the skin and tenderness. All patients received usual dose of Cephalosporins a day before surgery, then were maintained on same dose for 72 hours. Postoperative records of the temperature, signs of deep vein thrombosis and respiratory tract infection, and results of complete blood count, and urine analysis were made; any general or wound complication was managed accordingly.

Results

Patients were operated within 1-6 days (mean 3 days) from the day of admission. Out of 340 patients, single suction drain was used in 78 and two drains in 262 patients. The operative wounds where suction drains were used are detailed in Table 1. Distribution of patients' age, sex and associated medical illness is shown in Table. 2. Associated illness included hypertension, diabetes mellitus, bronchial asthma, ischaemic heart disease and epilepsy.

After removal of drain leakage from the exit site was observed in 31 elderly patients. This continued for less than 24 hours and settled spontaneously. Of these, bacterial cultures from the drain tips were positive in 24 patients. Out of these, 19 were from superficial drains (17 Group A and 2 Group B) and 5 from deep drains (Group A). But, clinically obvious infection was noted only in 4 of these 24 wounds. Fever (38-38.6C), leucocytosis and increased ESR with local signs of infection were noted in all these 4 patients. Following appropriate antibiotic therapy all of them settled within few days. By seventh post operative day no signs of inflammation were noted in 328 (96.4%) wounds. But, 12 (3.5%) showed local signs of inflammation (11 Group A and 1 Group B) including 4 wounds where frank wound sepsis was noted. This also settled spontaneously in few days time Swelling of the leg in 59 (17.3%) and ecchymosis in 40 (11.7%) patients were noted mostly in cases with fractures around hip and the thigh. None of the factors i.e., wound leakage, wound infection or inflammation , and swelling of the leg hampered the rehabilitation plan of the patients 7 patients developed post operative bronchopneumonia and 6 patients deep vein thrombosis. All these 13 patients had associated geriatric problems. Thus, delaying their rehabilitation for some days. Most of the patients showed some rise in body temperature during first three post operative days (not above 38 degrees C) which then settled down except in four patients where it persisted for a week. Post operative haemoglobin level dropped in some patients especially in elderly, unrelated to the volume of drainage, but stayed within the range of 9-10 gm% indicating blood transfusion in some. The volume of drainage varied from 30 ml .to 600 ml. There was marked variation in the amount of fluid withdrawn in each type of procedure and site of operation. Drainage was markedly less in wounds around the elbow, knee and the ankle and more in wounds of the hip and the thigh regions. The drain did not get plugged in any of the patients. In procedures of open reduction for fresh fractures, bone cyst and tumours or non-union where bone graft was used, radiological evidence of bony union was found in the usual expected time.

Discussion

To minimize the risk of wound infection and ensure primary wound healing and uncomplicated post operative course, wound care must include thorough haemostasis, adequate blood supply, removal of all necrotic material, obliteration of dead space and absence of wound tension[7]. As part of the process of inflammation, local swelling causes increase in local tissue tension automatically during the first 48 hours after injury. If unrelieved, this will jeopardize the local blood supply and subsequently lead to wound failure. Haematoma and infection can further increase this tension. Thereby, contribute to the unfavourable atmosphere for the wound healing[8]. Also, the fluids which collect in surgical wounds predispose to wound sepsis as they progressively lose the phagocytic capability[9]. Postoperative haematomas become an excellent culture medium for bacteria after 12-18 hours and upto 20% of such residual haematomas are contaminated[2]. So the evacuation of haematoma or seroma by closed drain during the first 48 hours after operation seems justified.

Table 1

Regional Distribution of Postoperative Wounds

Region	Number of Operations	Percentage of the total
Shoulder	8	2.35%
Arm	25	7.35%
Elbow	20	5.88%
Forearm	33	9.70%
Hip	90	26.47%
Thigh	53	15.58%
Knee	15	4.41%
Leg	56	16.47%
Ankle	37	10.88%
Foot	3	0.88%
Total	**340**	**100%**

The overall infection rate 1.1% in this series concurs with that of Waugh and Stinchfield,[4] although the 7% incidence of positive bacterial cultures was markedly less in this series as compared to 17% in their series. This can be explained on the basis that most of the wounds become contaminated by bacteria during major surgical procedures. But the development of a clinically obvious infection by low levels of contamination depends upon the local tissue and general host resistance, haematoma or seroma formation, and the type and virulence of the microorganism. Hence, a positive bacterial cultures does not confirm and a negative culture does not rule out wound sepsis unless the purulent material drains from the wound[4,9,10,11]. The infection in four patients with two drains (group A) and none in patients with one drain (Group B) could be attributed to longer surgical procedures in the former, where chances of bacterial contamination are more. The observation made by Cobb[3] that wounds with drains had more complications than without drains, is not supported by the findings from the largest group of 90 hip operations of this study, though the type of operations in the two studies were almost similar. The local resistance of the wound is much more important than general host resistance. This can be increased by using a subcutaneous suction drain[7].

Table 2

Summary of Observation

Group	Number of Patients	Percentage of total	Age in years (Range)	Sex		Assocaiated illness
				Male	Female	
A Two Drains	262	77%	11-110	169	93	45
B One Drain	78	23%	3-70	54	24	4
Total	340	100%		223	117	49

In our study three old and malnourished and one obese and diabetic patients got .wound infection. The old, malnourished, diabetic and obese patients are vulnerable to infections. Because, protein depletion may be associated with poor antibody response, and the vitamin and protein deficiencies produce decrease in phagocytic activity of leucocytes[12]. It has been reported that at Foothills 16% of malnourished surgical patients with clean wounds developed post operative wound infection[7]. Infections of extremities is common in diabetics, because of a high incidence of peripheral vascular disease causing hypoperfusion of the tissues which leads to impaired wound healing. The fatty tissue is relatively avascular and does not tolerate bacterial contamination. Thus, making obese patients susceptible to wound infection.[12]

Where contamination is expected or infection could be disastrous, Prophyloactic antibiotics are useful only when the drug is present in tissue fluids within three hours of bacterial contamination. For systemic antibiotic prophylaxis, most of the orthopaedic surgeons prefer routine use of Cephalosporins in total hip arthroplasty and for internal fixation of fractures with metal implants. Better results would be expected if antibiotics are started earlier than the day of operation and continued for a short period postoperatively[7,13]. Similar regimen was employed in this study.

The advantages of using a perforated tube is that the chances of getting plugged are less compared to a simple non-perforated one, where the mouth of the tube can become plugged with clot easily and result in inadequate drainage of the collecting haematoma. Further, a perforated tube effectively evacuates a wider area of the dead space.

The benefit of exit site of the tube being away from the main wound is that apposition of the wound margins is not affected. Hence, the natural process of wound healing proceeds undisturbed.

Functional end results obtained in all our patients were encouraging especially in hips treated with Dynamic Hip Screw or Prosthesis. It is possible that the effective removal of blood results in less swelling of wound and formation of less granulation tissue and scar. Therefore, facilitating the early mobilization of operated extremities.

Conclusion

Closed suction drains proved an ideal environment for primary wound healing as they allow egress of material foreign or harmful to a particular location, obliterate dead space decrease chances of infection, and thus, result in minimizing hospital stay and cost of the treatment. Also, by using two drains (superficial and deep) level of infection can be determinted and attacked accordingly.

Acknowledgment

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Atrophic Rhinopharyngolaryngitis-An Aetiopathological Study

Aziz A. Lone MS; Ahad A. Shiekh MS; Rather A. Rasheed MD; Rauf A. MS.

Abstract : *Atrophic changes of upper respiratory tract mucosa have diverse aetiological factors and considerable research has been directed towards the detection of primary cause as well as underlying predisposing factors. Accurate identification of aetiological factors and institution of an effective and most satisfactory form of management has been a challenge to Otorhinolaryngologists. The present study is carried on 400 patients attending the SMHS Hospital Srinagar having atrophic changes of the upper respiratory tract musosa of which 150 cases were confined to the Atrophic rhinitis, 200 cases of pharyngitis sicca and 50 cases of Atrophic laryngitis. Aetiological and pathological factors in this conection are considered.*

Key words:- *Atrophic rhinitis, Atrophic laryngitis, Pharngitis sicca,*

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Introduction

Atrophic rhinitis is a chronic degenerative nasal disease characterized by progressive atrophy of the mucosa and underlying bone of turbinates and the presence of a vicid secretion which rapidly dries and forms crusts having a characteristic foul odour, "Ozaena (a stench)" with abnormal patency of nasal passages. The disease starts at puberty and is more common in females, suggesting the possibility that some endocrine system disturbance is responsible for its development.[1] The patient mostly presents with nasal obstruction and epistaxis. Anosmia may be present. The exact aetiopathogenesis of primary atrophic rhinitis remains obscure. It is still widely labelled as idiopathic. Numerous organisms have been isolated from nasal swabs of these patients-Coccobacillus[2], Bacillus mucosus, cocco-bacillus faetidus ozaena, diptheroid bacilli and Klebsiella ozaenae, pseudomonas and proteus mirabalis.[3]

The Rhinologists are still striving to solve the problem of primary atrophic rhinitis, as far as its aetiopathogenesis and treatment is concerned. Endocrine dysfunction, congenital roomy nostrils and reflex sympathetic dystrophy syndrome (RSDS) have been mainly implicated as the causative factors.

Atrophic rhinitis seems to have multi factorial aetiology. No factor can be singled out to be totally responsible for this disease. All the three above mentioned factors play contributory role in the aetiopathogenesis of primary atrophic rhinitis.

Chronic sinus infection,[4] excessive destruction of nasal mucous membrane during surgery of nasal packing,[5] hot and dry working atmosphere and local chronic infections like lupus and rhinoscleroma,[6] have been implicated as local factors responsible.

A wide number of systemic disorders have been blamed as underlying predisposing factors, e.g. syphilis[7], leprosy[7], tuberculosis, chronic or repeated infections in upper or lower respiratory tract, chronic renal disease, liver disorders, hypothyroidism, diabetes Wegner's granulomatosus[8], malnutrition and anaemia[9]. Atrophic pharyngitis: is most often regarded as direct extension of atrophic rhinitis, granular pharyngitis, various conditions leading to mouth breathing lupus, excessive use of alcohol and smoking, Sjogren's Sydrome, Plummer Winson syndrome, Habitual use of condiments and highly spiced foods is an aggravating factor.

Atrophic Laryngitis: is characterized by atrophic changes in respiratory mucosa with loss of the mucous producing glands. It is usually part of an atrophic rhinitis.[10] Abuse of alcohol and tobacco, laryngeal

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lupus, nephritis, cardiac failure has been implicated as various factors responsible. The most common sites are false cords, posterior region and the subglottic region.

Material and Methods

The present study was conducted on 400 patients having atrophic changes of upper respiratory tract mucosa, who attended SMHS hospital Srinagar from August 1993 to January, 1995. The patients were subjected to detailed history and examination. Routine blood investigations, liver function tests, kidney function tests. thyroid function tests, VDRL, blood sugar (Random) were done in all cases. Bacteriological study of nasal swab was done in 150 cases of atrophic rhinitis.

Radiological study of chest, paranasal sinuses and cervical spine was done in all cases.

Histopathological examination of nasal mucosa was done in 110 cases of atrophic rhinitis and pharyngeal mucosa in 150 cases of pharyngitis sicca.

Observations

The cases were divided in three main groups:

Table N o. 1

		No. of Cases:
1.	Atrophic rhinitis	150
2.	Pharyngitis sicca	200
3.	Atrophic laryngitis	50
	Total	**400**

Out of 200 patients of pharyngitis sicca in study group, 24 patients were having atrophic rhinitis also, and out of 50 patients of atrophic laryngitis studied 29 cases were having atrophic nasal mucosal changes.

Maximum patients 55.0 per cent were in the age group of 10-30 years and 227 cases (56.75 per cent) were females.

207 (51.75 per cent) were from rural areas, 169 patients (42.25 percent) were housewives.

Maximum number of patients (78.25 per cent) presented during winter season (from October to March months) of the study period.

Atrophic rhinits group: Out of 150 cases of atrophic rhinitis 85 cases (56.67 per cent) presented with history of nasal blockage, 23 cases (15.33 percent) with faetor and 9 cases (6.0 percent) with maggots.

130 patients (86.67 percent) were having poor socio-economic status. Recurrence of symptoms was observed in 32 out patients (21.33 percent) in October to December months.

Table No. 2

	No. of Cases	Percentage
1. Anaemia	60	40.00
2. Lepromatous leprosy	8	5.33
3. Pulmonary tuberculosis	8	5.33
4. Thyroid hypofunction	18	8.57

Radiological Study

Table No. 3

1. Bilateral hazy maxillary sinuses	66	44.00
2. Antral mucosal thickening	14	9.34
3. Straightening of cervical spine curvature.	75	50.0

Bacteriological Study

Table No. 4

1. Klebsiella	34	33.67
2. Pseudomonas	28	18.67
3. Pseudomonas + E. Coli	10	6.67
	72	

Histopathological study

Table No. 5

1. Surface squamous epithelium	20	18.18
2. Squamous metaplasia	5	4.54
3. Chronic cellular infiltrate	60	54.54
4. Atrophy of seromucous glands	5	4.54
	90	

Pharyngitis Sicca Group

134 Cases (67.0 percent) were in age group of 21-40 years.

Table No. 6

1. Poor dietary habits	60	30.0
2. Excessive spices intake	61	30.50
3. History of smoking	70	35.00
4. Use of snuff	9	4.50

164 Cases (82.0 per cent) presented during winter months of the year (October to March months). Recurrence of symptoms was found in 104 cases (52.0 per cent) during winter months of the year.

Table No. 7

Local examination	No. of Cases	Percentage
1. Bilateral hypertrophied turbinates.	69	34.50
2. DNS with hypertrophied turbinates on roomy side of nose.	63	31.50
3. Atrophic rhinitis	24	12.0

Radiological study

Table No. 8

1. Bilateral hazy maxillary sinuses.	68	45.33
2. Unilatemal hazy maxillary sinus.	8	5.33
3. Bilateral antral mucosal thickening.	8	5.33
4. Unilateral opaque antrum	6	4.0
5. Straightening of cervical spine curvature	58	38.67

Histopathological study

Table No. 9

1. Chronic cellular infiltrate	54	36.00
2. Fibrosis in lamina propria	35	23.33
3. Squamous metaplasia	4	2.67

Atrophic Laryngitis Group

Main complaint was hoarseness of voice in 35 (70.0 per cent). 4 cases (8.0 per cent) presented with respiratory distress and in 3 cases (6.0 per cent), haemoptysis was seen. In 29 cases (58.0 per cent) atrophic changes of the nasal cavity had spread to the larynx producing atrophic laryngitis.

On indirect laryngoscopy, crusts were found in glottic region, covering posterior part of both cords. In 24 cases (48.0 per cent).

X-ray paranasal sinuses (Water's view) showed chronic maxillary sinusitis in 32 cases (64.0 per cent). X-ray cervical spine (Lateral view) showed straigtening of cervical curvature in 23 cases (46.0%) and 14 cases (28.0%) showed early changes of cervical spondylosis.

Discussion

No single or definitive cause has been attributed for atrophic rhinitis till now, but multiple causative factors have been held responsible for this ailment.

Primary atrophic rhinitis starts around puberty and is more common in females, favours the theory of endocrine dysfunction to have some definitive role in the aetiopathogenesis of disease.[1]

Out of 150 cases of atrophic rhinitis, 20 cases (13.34) had wide nostrils with depressed bridge. Nostrils were directed more forwards, so direct impingment of the inspiratory stream on the turbinals, leading to subsequent collapse of the turbinates. The study conducted favours Zaufal mechanical theory of congenital spacious nasal cavity.

Reflex Sympathetic Dystrophy Syndrome (RSDS) seems to be a causative factor, is thought to be caused by chronic nasal infection and repeated trauma to nose during childhood. It appears that injury caused by the impact of respiratory stream on the vascular tissues, is both an initiating factor, causing sympathetic dystrophy by its mechanical trauma and perpetuating one by causing collapse of the turbinals and further dystrophy.

130 cases (86.67 percent) of atrophic rhinitis belonged to poor socio-economic status. In 88.0 percent cases the daily diet was poor in vitamins, iron and protein supplementation. Our observation is consistent with the observations made in Papua New Guinea and other developing countries.

Chronic sinus disease was present in 66 cases (44.0 percent) and was confirmed by antrum wash with mucopurulent washout. Our findings coincide with Schonemann.[4]

In our study 10 cases (6.67 percent) reported with complaints of nasal obstruction and crusting within the 2 to 3 year follow up period of septoplasty with turbinectomy, which is consistent with the findings of Martinez et al 1983, who observed crusting in 6.90 percent cases during a 3 year follow up period.

Iron deficiency anaemia has been observed in 60 cases (40.0 percent) of atrophic rhinitis. The haemoglobin percentage ranged from 3.8 to 10.0 gm%. Our findings coincide with that of Bernat.[9] 68.67 percent cases presented during winter months of the study period, as the ambient temperature decreases cilliary activity leading to stagnation of secretions and crusting, our study supports the view point that atrophic rhinitis is more common in females and illitrate rural population with poor personal hygiene and health education.

Cold climate seems to have a significant role in the aetiopathogenesis of atrophic changes in the upper respiratory tract mucosa.

In our study 8 patients (5.33 percent) were having lepromatous leprosy. Low standard of living and poor hygienic conditions in our set up are responsible for the existence of leprosy which acts as one of the contributory factors leading to atrophic rhinitis.

8 cases (5.33 percent) were having pulmonary tuberculosis. In our study (74.67 percent) cases were having chronic renal disease and 6 cases (4.0 percent) were having chronic liver disease, giving rise to atrophic changes in nasal mucosa.

There seems to be a relation between cervical spine curvature changes and the atrophic changes of upper respiratory tract mucosa, whether it is a cause or effect needs further study.

On histopathological study of nasal mucosa 5 patients (4.54 percent) were having atrophy of seromucus glands, 5 patients (4.54 percent) were having squamous metaplasia and 60 patients (54.54 percent) were having chronic cellular inflammatory infiltrate which suggests a humoral mediated immune process. Our findings were consistent with observations made by Latif et al.[11]. Altered cell mediated immunity in atrophic rhinitis was demostrated by Fouad et al.[12]

In 28 cases (18.67 percent) pseudomonas and in 34 cases (22.67 percent) Klebsiella was isolated from nasal swab bacteriological study. 164 cases (82.0 percent) of pharyngitis sicca presented during winter months explaining a definite seasonal relationship. During cold climate inhalation of dry cold air with ambient temperatures decrease the ciliary activity leading to stasis of secretions in the nose and crusting which produces secondary effects on pharynx leading to sicca condition. The same observation was made by several authors who concluded that mucociliary clearance falls as the ambient temperature drops below 37°C and that mucociliary surfaces directly exposed to dry air demostrate reduction in transport function.[13] Chronic nasal obstruction due to any obstructive pathology in the nose leads to mouth breathing which causes dryness of pharyngeal mucosa and crusting.

61 cases (30.50 percent) of pharyngitis sicca were using high spicy foods and was labelled as an aggravating factor. In 35.0 percent cases history of smoking was present. The various constituents in tobacco lead to vaso-constriction of the arterioles and venules leading to local ischaemia with metaplasia and keratinization of the surface epithelium. The depressant effect of tobacco smoke on ciliary activity has been demonstrated by various authors.[14]

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Helicobacter Pylori Infection in Endoscopic biospy Specimens of Gastric Antrum: Laboratory Diagnosis and Comparative efficacy of three diagnostic tests.

G.M. Malik, MD, FACG; S.Kadla, MD; M.Mubarik, MD; T. Hussain, MD; G. Jeelani, MD; A.R. Khan, MD.

Abstract : Helicobacter pylori infection was sought in 150 patients referred for upper G.I. endoscopy. Multiple (about six) biopsy specimens were taken from each patient. Two biopsy specimens were subjected to one minute endoscopy room test-OMERT (a modifed from of ureas test), two were sent for histopathological analysis, where multiple sections were subjected to Giemsa staining and two were sent for microbiological evaluation after Gram's staining of heat fixed biopsy material. Helicobacter pylori positivity using histology, microbiology and OMERT was observed to be 33.33%, 30% and 26.67% respectively. However, overall 40% patients were infected when the results from three test procedures were combined, as H. pylori positivity was repeated more than once by these procedures separately. Histology was found to be superior to other two tests in our study, especially when multiple biopsy specimens (at least two) with as many sections were studied for H. pylori. Further, we evaluated H. pylori status in relation to histological findings by these tests.

Keywords : H.Pylori Infection, Endoscopic biopsy, OMERT.

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Introduction

In 1983, Warren and Marshall reported unidentified curved bacilli in the gastric antral biopsies from patients with active gastritis and peptic ulcer disease.[1] This becteria was Campylobacter pylori. Subsequently its name was changed to Helicobacter pylori.[2,3] Currently there are many diagnostic tests for detection of infection with this organism, but there is no commonly acknowledged "gold standard" method for diagnosing H. pylori infection. The best way to detect H. pylori in histological sections would be to examine suitably stained sections of a biopsy specimen under high power of microscope. In addition to this, the other methods like urease test and microbiological evaluation also establish the diagnosis of H. pylori infection.[4]

The aims of our study were: (1) to determine H. pylori infection in endoscopic biopsy sepecimens of gastric antrum, using three available test procedures separately and in combination; (2) to determine which test among the three is the most sensitive and specific; and (3) to determine H. pylori status in relation to histological findings by the above tests.

Material and Methods

The study comprised 150 patients referred for routine upper gastrointestinal (GI) endoscopy. Their mean age was 34.80±10.19 years with 125 males and 25 females. The main indication for biopsy was dyspepsia. Patients who had taken antibiotics, H_2 blockers, colloidal bismuth or omperazole one to two months prior to endoscopy were not included in the study.[5,6] From each patient six biopsies were taken from the gastric antrum within 5 cms of pylorus. These biopsy specimens (two chips each) were subjected to following test procedures.

One minute endoscopy room test (OMERT)

In this test, two biopsy specimens were put in one ml of 10% W/V freshly prepared urea solution in deionized water (PH 6.8) at room temperature. Two drops of 1% phenol red were added to above solution as an indicator. A change in colour from yellow to pink observed 1-5 minutes after addition of indicator was taken a positive test (i.e. H. pylori present), whereas absence of such a colour changes or change of colour after 5 minutes was taken as negative test.[7]

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Histological Analysis

Two antral biospy specimens from each patient were fixed in 10% buffered formalin. Paraffin wax sections were cut after routine processing.[4,8,9] They were stained with May-Grunwald-Giemsa stain.[10] The entire epithelial surface of all stained sections was examined under oil imersion by one observer who did not know the results of other test procedures. The presence of curved bacilli in the vicinity of gastric epithelium was taken to be indicator of H. pylori infection. All the sections of paired biopsy specimens were studied for presence or absence of the organism. Further the histology of gastric mucosa was also studied in relation to H. pylori.

Microbiological analysis

Two biopsy specimens were rubbed on a dry glass slide, heat fixed and then stained with Gram's stain, and finally studied for the presence of H. pylori under light microscopy.[2]

Ethics: All subjects gave informed consent for the collection of biopsy tissue. Human experimentation guidelines of the "Decleration of Helsinki" were followed.

Results

Of 150 patients biopsied, overall 60 (40%) were infected when the results of the three test procedures were added. The results were added because H. pylori positivity was represented more than once by three test procedures separately. Helicobacter pylori positivity was observed to be 50 (33.33%) , 45 (30.00%) and 40 (26.67%) using histology, microbiology and OMERT respectively (Table-I) Ten patients detected positive by histology and OMERT were negative by microbiology. One the other hand, 10 patients detected negative by histology were positive by microbiology. All 40 patients detected positive by OMERT, were also detected positive by histology. One the other hand, three patients detected positive by OMERT were negative by microbiology.

The comparative sensitivity, specificity and predictive values of the histology as compared to OMERT and Gram's staining are represented in table-II.

The histopathological examination of the biopsy smears revealed changes of chronic superficial gastritis, chronic active gastritis in some patients, whereas majority of patients had normal gastric mucosa. The H. pylori status in relation to histopathological changes of gastric mucosa is revealed in talbe-III.

From each biospy specimen about 3-8 Giemsa stained sections were made. Each section was examined under oil immersion. Thirty percent of the infected patients had H. pylori present in all the sections of biopsy specimens and the remaining 70% had the organism present in one biopsy section other sections being negative.

Discussion

Currently many different diagnostic tests exist for detecting H. pylori infection. Each test has its own merits and demerits in terms of indication, sensitivity, specificity, cost and time[5,11]. Many different protocols have been used to detect H. pylori in biospy specimens. The protocols include urease test, histology, microbiology, culture and polymerase chain reaction. Currently polymerase chain reaction is experiemental and gives lot of false positive results which therefore, limits its use as a gold standard. Culture of the biopsy specimen cannot be used routinely as it is time consuming and is very difficult to maintain the strict anaerobic measures.[3,6] ELISA serology for the diagnosis of H. pylori is done by assessing the IgG antibodies and has sensitivity and specificity of 95%. But, the test is costly and has a false psitive result of 10%.[10,11] C^{13} urea and C^{14} urea breath tests are highly specific (98%) and very sensitive (95%). But these tests are costly and therefore cannot be advocated for routine use. Thus, the choice lies in ureasetest, histology and microbiology.[4,5] Our study was also aimed at these three test procedures.

Ureas test detects the urease activity of the organism. Conventional urease test has sensitivity and specificity of 84% and 86% respectively. Various modifications of the conventional urease test have taken place from time to time simply to increase the sensitivity and specificity. The one such modification is one minute endoscopy room test (OMERT) which has sensitivity of 91% and specificity of 100%.[7] Variations do exist in the methods used to detect H. pylori by microbiology. The results are excellent by rubbing the biopsy specimen over a dry glass slide rather than cutting or grinding the biopsy specimen.[4,5]

In our study, we found that OMERT was more sensitive than the microbiological method. Why false positive results are seen with OMERT and microbiological methods, is not known. It has been claimed that 5-10% patients have low number of H. pylori which cannot be detected by urease test.

Table-I: Diagnostic test results in 150 patients biopsied for H. pylori infection

	Test procedure	H.pylori positive patients	Percentage
1.	OMERT	40	26.67
2.	Microbiology (Gram's staining)	45	30.00
3.	Histology	50	33.33
4.	Test procedures in combination	60	40.

OMERT = One minute endoscopy room test

Table- II Comparative efficacy of diagnostic tests for H.pylori

	Test procedure		
Variable	Histology	OMERT	Gram's staining
Postive	50	40	45
Negative	100	100	105
False positive	-	10	15
False negative	-	10	10
Sensitivity	-	80%	77.78%
Specificity	-	91%	85.71%

Note: The absence of false positives and false negatives, when H. pylori status was observed by histology. Further taking sensitivity and specificity by histology as 100% (standard), the same was observed to be much less in case of OMERT and Gram's staining.

Table-III: Histological findings and H. pylori status of biopsy specimens (n=150)

		H. Pylori positive by		
Histology	No. of cases	Histology	OMERT	Gram's staining
Normal gastric mucosa	100(66.66)	25 (25.00)	15(15.00)	15 (15.00)
Chronic active gastritis	30(20.00)	20 (66.66)	25(83.33)	20 (66.66)
Chronic Superficial gastritis	20(13.33)	05 (25.00)	05(25.00)	05 (25.00)
Total	150	50(33.33)	45 (30.00)	40 (26.66)

Histology has been used as a diagnostic tool fo H. pylori. Various stains like haematoxylin and eosin, Giemsa, Gram's, 1% methylene blue, Warthin Starry silver method and fluorescent stains.[3] As per current recommendations, Giemsa staining is the best stain, as it is cheap, less time consuming and diagnostic yield is increased as compared to other staining procedures.[11] Barry J Marshall advocates "If the H. pylori diagnosis is going to make an important contribution to management, then the most sensitive test should be used. Currently this is histology".[11] This is in confirmity with our observation that histology (Giemsa staining) detected most of the infected patients who underwent gastroscopy in our study. Histology, in addition to detection of the organisms, also helps in establishing the diagnosis of associated gastritis (if present) in the biopsy specimen.

The distribution of H. pylori in gastric mucosa is patchy. Therefore, the antral biopsy specimens may not be containing the organisms at all and hence H. pylori cannot be diagnosed in such a condition. In accordance with this study we, like others[6], also believe that multiple biopsies (at least two) from multiple sites of the stomach, should be taken in order to increase the diagnostic yield. Further, we observed that the chances of detecting H. pylori increased when maximum sections of the bioplsy specimens were studied, that can again be explained on the basis of patchy distribution of H. pylori.

Microbiological analysis of gastric biopsy specimens was not sensitive as OMERT or histology in our study. Other disadvantage with such evaluation is that it does not provide information about the presence of gastritis, which is tru with OMERT as well. Thus, histology is superior to other test procedures and we also consider it to be the gold standard for diagnosis of H. pylori infection in confirmity with some ealier reports.[4,11] Further, multiple biopsy specimens must be taken (at least two) from multiple areas of the stomach and as many sections as may be available should be studied to ensure optimal detection of H. pylori. The increased association of H. pylori with chronic active gastritis as compared to the other two histopathological findings as observed in our study, is in confirmity with earlier reports[1,2].

Acknowledgement

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Comparison of different surgical techniques for reconstruction of hypospadias - A six years experience with 103 patients

Syed Qawnain, M.S; N.A. Wani, M.S.; F.R.C.S.; M.Ashraf Darzi, M.S.; M.Ch.; Syed Sajjad Nazir, M.S.; Nissar Chowdhary, M.S.; Omar Javed Shah, M.S.

***Abstract** : This study was carried out in 103 patients of hypospadias who were admitted in SKIMS over a period of six years from Dec. 1983 to Nov. 1989. The patients were evaluated thoroughly and repair was carried out by various surgical techniques. The results were analysed to evaluate various techniques of hypospadias repair. 57.29% of our patients had distal variety of hypospadias and 45% had associated chordee. Associated anomalies were seen in 19% of patients. MAgpi procedure was found procedure of choice for glanular, coronal and subcoronal hypospadias and was associated with low complication rate. For proximal varieties and for previously failed operations multistage procedures were performed. The overall complication rate was 23.40% and overall results based on cosmesis and function were excllent in 6.22%. Satisfactory in 36.73% and failure in 3.05%. No single procedure was found suitable for all types of hypospadias.*

Key words: Hypospadias, MAgpi procedure, Chordee, Multistage procedure.

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Introduction

Hypospadias is one of the common congenital anomalies in which urethra ends on the ventral suface of penis anywhere between glans and perineum. It forms one of the major surgical problems in children. Incidence being 1 in 300 male new borns and ranges in severity from simple glanular to penile and more severe scrotal or perineal forms. The etiology is obscure and is thought to be related to abnormalities of androgen production and timing or receptor function during male sexual differentiation in the early period of gestation. Chordee is usually associated with proximal varities of hypospadias. Other abnormalities associated with hypospadias are hernia, hydrocoele, undescended tests, myelomeningo coele, sacral agenesis, imperforate anus and upper urinary tract anomalies. The basic aim of hypospadias surgery is correction of chordee and reconstruction of urethra which is free from fistulae.

Directable urinary stream, ease of coitus and cosmetic satisfaction are achieved by repair. There are many techniques of reconstruction single or multistage which give varying degree of success. Surgical procedures are fraught with complication like wound dehiscence, fistulae formation, strictures and urethral diverticulae.

Material and Methods

This study was conducted on patients of hypospadias who were admitted in the department of Plastic Surgery SKIMS, Soura, Srinagar Kashmir (J&K) India over a period of six years from Dec. 1983-Nov. 1989. A total of 103 patients were studied. The patients were evaluated thoroughly and repair was carried out by various surgical techniques. The results of various methods were analysed to evaluate various techniques of hypospadias repair. A detailed history and examination was carried out. Routine investigations are done and some specific investigations like sex chromatin study, urinary keto steroids and gonadal biopsy were performed in patients of ambiguous genitalia to clinch a definite diagnosis.

Timing of surgery: Meatal stenosis was treated

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promptly and meatatomy performed at any time at which patient reported to hospital. Parents were advised not to get their child circumcised. Chordee was first target of surgical correction and was usually undertaken between 2 to 3 years of age. Unless patient presented late urethral reconstruction was done at the age of 4 to 5 years or six months after the first operation in children more than 5 years of age in order to allow tissues to recover fully from the effects of first operation. The following surgical procedures were undertaken for repair and reconstruction of hypospadias.

a. Anterior meatatomy for meatal stenosis
b. For chordee correction three methods were used.
  i. Byars method
  ii. Nesbits method
  iii. Local rearrangement of tissues

Byars and Nesbits methods were used for major degrees of hypospadias with chordee. Minor degrees of chordee were treated by local rearrangement of tissues.

c. Urethroplasty: Depending upon degrees of hypospadias and availability of local skin following techniques of urethral reconstruction were used:
  1. MAgpi (meatal advancement and glanuloplasty)
  2. Horton-Devine flip. flap
  3. Kilners modification of ombredanes
  4. Byars of modified Denis Brownes method
  5. Cecil culp method

MAgpi, Horton-Devine flip flap and some cases of Kilners modification of ombredances method were performed in single stage while all other techniques were carried out as multistage procedures.

Results of surgery and followup: All patients were summoned up periodically in follow up clinic to assess the results of surgery. Any post operative complication early or late were recorded. Thorough local examination was done and post operative photographs were taken for comparing results of surgery.

Results were rated as follows:-

1. Excellent: Cosmetically acceptable penis with glanular meatus without residual chordee and direct forceful urinary stream.
2. Satisfactory: Mild to moderate deficiencies like excessive penile skin, presence of dog ears, retracted meatus or small patent uretherocutaneous fistula.
3. Failure: Repair was considered as failure if there was complete dehiscence of neourethra and necrosis of flap which required total reconstruction.

Results

The results of reconstruction were evaluated post-operatively and were observed as follows:

A) Release of chordee: Chordee correction was carried out by three methods. Table I shows methods of release performed in various patients of our series.

Method and Chordee	No. of pts.	%
Byars method	26	25.24
Nesbits method	11	10.68
Local rearrangement of tissues	10	9.70
Total	**47**	**45.62**

4 Patients hád residual chordee and were subjected to release of chordee.

B. Urethroplasty:

Of 103 patients, 98 underwent 5 different kinds of urethroplasties. Out of the rest 5 cases, 2 cases of ambiguous genitalia did not report after preliminary investigations and determination of sex by sex chromatin study, laproscopy and gonadal biopsy. One case of ambiguous genitalia underwent orchidopexy and chordee correction and is waiting for urethroplasty. Amongst other two cases one patient of isolated chordee without hypospadias required only chordee correction and another patient of glanular hypospadias needed only anterior meatoplasty.

Table 2
Shows different kinds of repairs carried out of 98 patients

Type of surgical procedure	No. of patients	%
MAgpi/Meatal advancement & glanuloplasly	41	41.85
Horton-Devine flip-flap	3	3.06
Kilness modification of ombredanne	26	26.52
Byars modification of Danis Browne	24	24.49
Cecil culp	4	4.08
Total	**98**	**100.00**

Table 3

Type of repair	No. of pts.	%	Glandular	Coronal +sub coronal	Distal penile	Mid shaft + proximal penile	Penoscrotal	Scrotal	Perineal
MAGPi	41	41.85	-	41	-	-	-	-	-
Horton Devine flip flap	3	3.06	-	1	2	-	-	-	-
Kilners modification of ombredanne	26	26.52	-	1	13	12	-	-	-
Byars modification of Denis Browne	24	24.49	-	-	-	18	6	-	-
Cecil culp	4	4.08	-	-	-	-	3	-	1
Total	98	100	-	43	15	30	9	-	1

Table 3 reveals type of repair in relation to each variety of hypospadias. Post-operative complications

Table 4

Shows various complications seen in different methods of chordee correction

Complication	Total		Byars method		Nesbits method		Local rearrangement of tissue	
	No	%	No	%	No	%	No	%
Residual chordee	4	3.92	2	1.96	-	-	2	1.96
Infection	4	3.92	2	1.96	2	1.96	-	-
Wound dehiscence	1	0.98	-	-	1	0.98	-	-
Necrosis of flap	7	6.86	5	4.90	2	1.96	-	-

Complications of definite repair

There was no mortality seen in our series of 103 patients. However, certain complications were seen as shown in table 5. The overall percentage of complications were 23.47.

Complications	Total number	MAGPI repair		Horton-Devine flip-flap		repair		Byar's method		Cecil culp repair	
	No	No	%	No	%	No	%	No	%	No	%
Infectios	4	-	-	-	-	2	2.04	2	2.04	-	-
Flap necrosis leading to wound disruption	3	-	-	-	-	2	2.04	1	1.02	-	-
Fistula	6	-	-	1	1.02	1	1.02	3	3.06	1	1.02
Stenosed meatus	2	-	-	-	-	1	1.02	-	-	1	1.02
Retracted meatus	8	3	3.06	-	-	4	4.08	-	-	1	1.02

Follow up period: Of 103 patients, 98 were operated and reported for follow up. The breakdown of followup of these patients is shown in table 6.

Table 6

Followup period	No. of pts.	%
3 months - 6 months	8	8.17
6 months - 1 year	60	61.23
1 yr. - 5 yr.	15	15.30
3 yr. - 5 yr.	5	5.10
5 yr. - 6 yrs.	10	10.0
Total	98	100.00

Majority of our patients had a follow up period of more than six months

Results of surgical reconstruction

The results of reconstruction by various methods performed on 98 patients are shown in table 7.

Table 7

Type of repair	No. of patients	Excellent		Satisfactory		Failure	
		No.	%	No.	%	No	%
MAGpi	41	38	92.68	3	7.32	-	-
Horton-Devine flip-flap	3	2	66.66	1	33.34	-	-
Kiners modification of ombredanne	26	5	19.23	19	73.10	2	7.67
Byars modification of Denis Browne	24	13	52.17	10	41.66	1	6.17
Cecil culp	4	1	25.00	3	75.00	-	-
Total	98						

Overall - grading of results:

Overall results of all the five different methods of repair are shown in table-8.

Table 8

Grading of results	No. of pts	%
Excellent	59	60.21
Satisfactory	36	36.73
Failure	3	3.06
Total	**98**	**100.00**

Discussion

A plethora of techniques have been described for correction of hypospadias which gives varying degrees of success. During the last two decades dramatic advances have been made in this state of art and science of hypospadias repair. For this we own much to the work of Horton and Devine (1981 & 1977)[5,6] the Hodgson (1970)[9] and with a operative artificial erection test introduced by Gittes and Mclaughlin (1974)[8]. Over the last several years increasing attention and emphasis have been placed upon performing corrective operation in a single stage thereby foregoing multiple hospitalisation and anaesthesia.

Culp (1954) advocated chordee correction between 18 months to 2 years of age. In our series chordee was corrected before 2 years of age in 4% of cases. 70% of cases presented after 5 years of age. Complications after chordee correction were encountered in 16 cases in our series Flap necrosis was the commonest complication seen followed by residual chordee, infection and wound dehiscence as shown in table 4. Incidence of flap necrosis was higher in these cases treated by byars techniques.

Creevy (1958)[3] reported one instance of residual chordee, two strictures and one case of wound dehiscence. After 78 straightening operations Culp (1959)[4] acknowledged three persistent chordee, six neonatal strictures and four wound dehiscene.

Kumawat et al 1980[11] in a series of 45 patients noticed residual chordee in nine cases, infection in 3, wound dehiscence in one and necrosis of flap in one patient. The draw back with nesbits methods was formation of redundant dog ears.

Only complication in 41 MAgpi repairs was meatal retraction in 3 cases (7.3%).

Duckett (1981)[7] reported a complication rate of 2.5% in a series of 207 MAgpi repairs in the form of wound dehiscence in 4 patients and fistula in one patient.

Levine et al 1984[12] reported no complication in a series of 86 cases.

Ozen and Whitaker (1987)[14] in a series of 67 MAgpi repairs reported a complication rate of 91% in the form of retracted meatus in 4 cases, stenosed meatus in one case and residual chordee in one case.

Horton-Devine flip flap was used in 3 patients in our series out of which 1 case (33%) developed complication in the form of fistula at the site of reapproximation of lateral glanular flaps. Mills and his associates (1981)[13] noticed complications in 4 patients after 15 Horton-Devine flip flap repairs in the form of fistulas on 3 patients and meatal stenosis in one patients.

Kilnerand Peat (1950)[10] found modified ombredannes procedure suitable for those casesin which urethral orifice after chordee correction was distal to mid shaft. This type of procedure was done in 26 cases of mid and distal shaft hypospadias. All sorts of complication was seen after this procedure i.e. retracted meatus in 4 cases (4.087), ischaemic necrosis of flap leading to wound disruption in 2 cases, fistula in one and stenosed meatus in one (1.02%) cases. Byars modification of Denis Browne was used in 24 (24.79%) patients of proximal hypospadias. After this procedure infection was noted in 2 (8%) of patients, wound disruption in one (4%) and fistula formation in 3 (10%) patients.

Byars 1955[1] reported 12 fistulas after 52 cases and only 4 fistulas after 144 cases in 1960.

Kumawat 1980[11] reported one case of complete dehiscence, 1 fistula formation and thinning of stream in one patient after 15 cases of byars urethroplasty.

Cecil culp meateoplasty was performed on 4 patients with extensive scarring following previous unsuccessful surgery and three cases of complications were seen. One had stenosed meatus (25%) one had retracted meatus (25%) and one had fistula formation.

Kumawat et al (1980)[11] reported 31.3% of fistula formation in his series and Creevy 1958[3] 7.6% of fistula formation after cecil culp meatoplasty.

Conclusion

There is no one good method of repair for all types of hypospadias. A technique must be adopted for each individual patient. Therefore surgeon ought to be proficient in preforming a number of procedures in order to be prepared for all possible even eventualities. Regardless of the method followed, successful hypospadias repair requires careful design, impeceable technique and meticulous attention to detail. Having used five different techniques of urethroplasties on 98 cases of different varities of hypospadias, we conclude that they cannot replace each other. Their merits and demerits are to be considered in the light of degree of hypospadias and many technical factors involved. From the results of various techniques used one feels that:

i. MAgpi procedure is wonderfully reliable and complication free, best suited for patients with glanular, coronal and subcoronal hypospadias.
ii. Horton-Davine flip flap repair is best suited for patients with distal hypospadias.
iii. Kilners modification of Ombreadane method is recommended for those cases of hypospadias in which meatus is at distal to mid shaft of penis after chordee correction with prepuce intact. However, this method was not found to be satisfactory cosmetically.
iv. For proximal varieties of hypospadias a multistage repair should be elected viz Byars procedure where uretheral meates lies proximal to mid shaft of penis and cecil culp

urethroplaslty in cases where circumcision has been performed or where there have been previous unsuccessful operations resulting inscarring and deficiency of skin on ventral surface of penis.

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Missile Injuries of the head A SKIMS experience

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***Abstract** : 94 patients of missile injuries were admitted to the department of Neurosurgery, Soura, Srinagar over a period of seven years (January 1990- December 1996). Retrospective study was carried out to analyse the management and outcome of these patients.*

After initial aggressive resuscitation, patients were subjected to computerized tomographic scanning. Rapid surgical debridement was done in most of the patients, except for a few, who succumbed to the injuries, before any surgical intervention was possible. Patients with low GCS score had poor outcome. Outcome progressively improved as the GCS score improved.

Key words: Missile injuries, Glasgow Coma Scale, Computerized tomographic study.

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Introduction

Earlier studies conducted regarding missile injuries to the head, generally concluded with the observation that nearly half of wartime deaths are due to penetrating craniocerebral trauma[1,2,3]. However, in the civilian population, firearm injuries to the head are second only to vehicular accidents as a cause of head injury related deaths.[4] The annual incidence of gunshot wound (GSW)- related head injury deaths in U.S. has been estimated at 2.4 percent 100,000 or approximately 6,000 deaths per year.[4]

Accidental firearm injuries also contribute significantly as a cause of such deaths. Stress has been laid on debridement of necrotic tissue, removal of accessible in-driven bone and missile fragments, not at the expense of increased neurological deficit or loss of significant amounts of potentially viable cerebral tissue. Significant mass lesions should be evacuated and proper haemostasis achieved, followed by meticulous dural and scalp closure, utilizing grafts or rotational flaps. Strict applications of these principles led to an operative mortality of approximately 10% during the Vietnam War.[5,6,7,8]

The advent and widespread availability of CT has had profound effect on the management of penetrating wounds. There has been number of advances in the intensive care management of such patients. Broad spectrum and relatively nontoxic antibiotics, that exhibit good CSF penetration are now available which prevent post injury infections.

The morbidity and mortality rates associated with missile injuries of the head, unfortunately have remained high inspite of all the advances. Generally GSWs to the brain are n ot compatible with life, and victims die at the site of accident or soon after arrival at an emergency centre.[9] Current advanced medical and surgical treatment available even cannot salvage many of these patients.[10,11]. Patients with better GCS score have good outcome.

Meterial and Methods

94 patients of penetrating injury to the head following missile injury were admitted to department of Neurosurgery, Soura Srinagar from Jan 1990 to December 1996. These injuries were either caused by firearm or flying shrapnel fragments from explosive devices.

These patients were resuscitated in the accident and emergency department. Comatose patients were intubated and large-bore intravenous lines were placed and fluid resuscitation begun. Resuscitation was continued according to advanced trauma life support guidelines. Every effort was made to recover and maintain stable vital signs.

Pateints were thoroughly evaluated by GCS score and brain stem functions. Patients were thoroughly investigated. Blood grouping and cross matching was done besides other laboratory investigations which included haemogram, coagulogram, serum chemistry,

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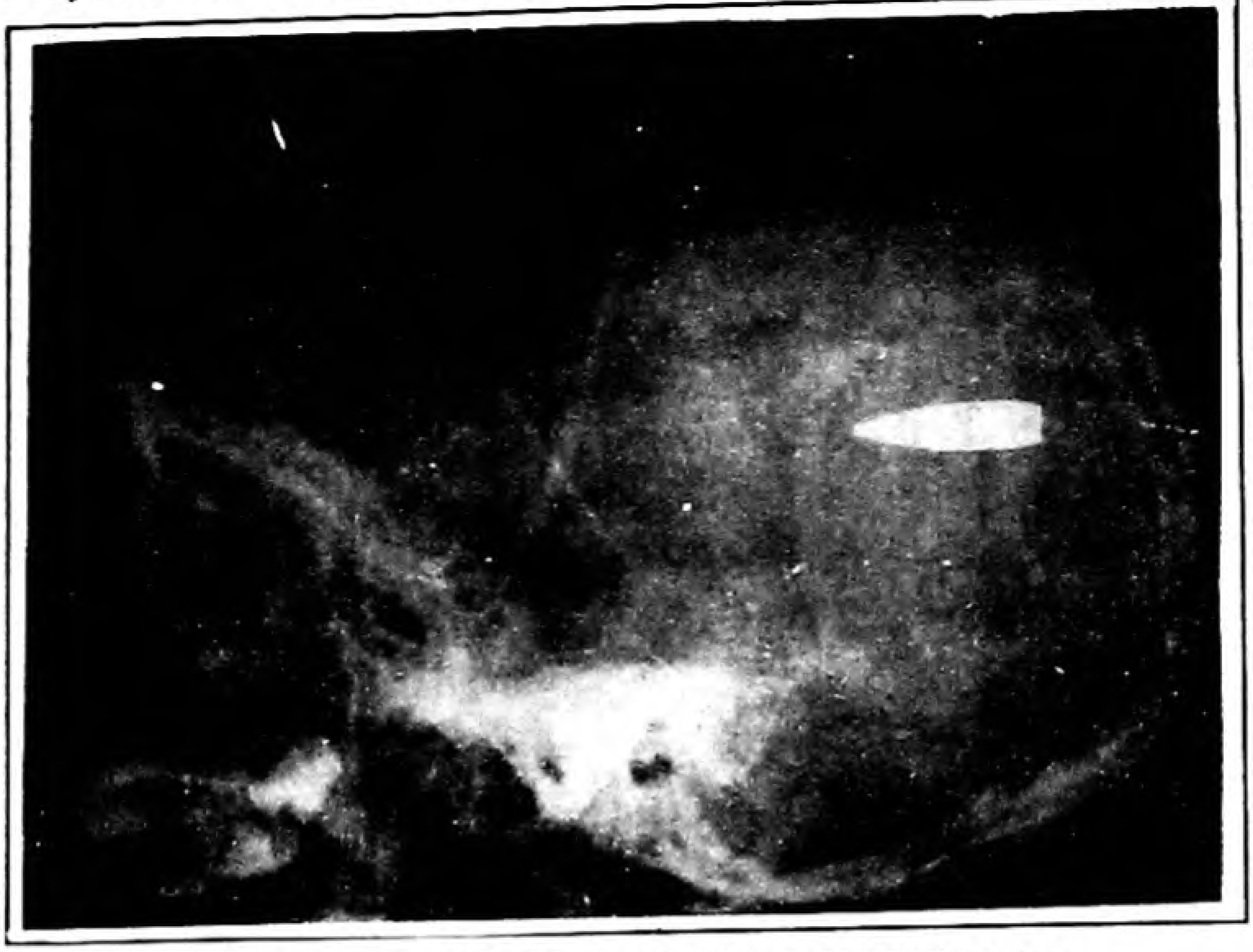
blood gas analysis and urine examination. Plain radiology of the skull and x-rays of other involved parts of body were done. Computed tomographic (CT) scan of head was performed.

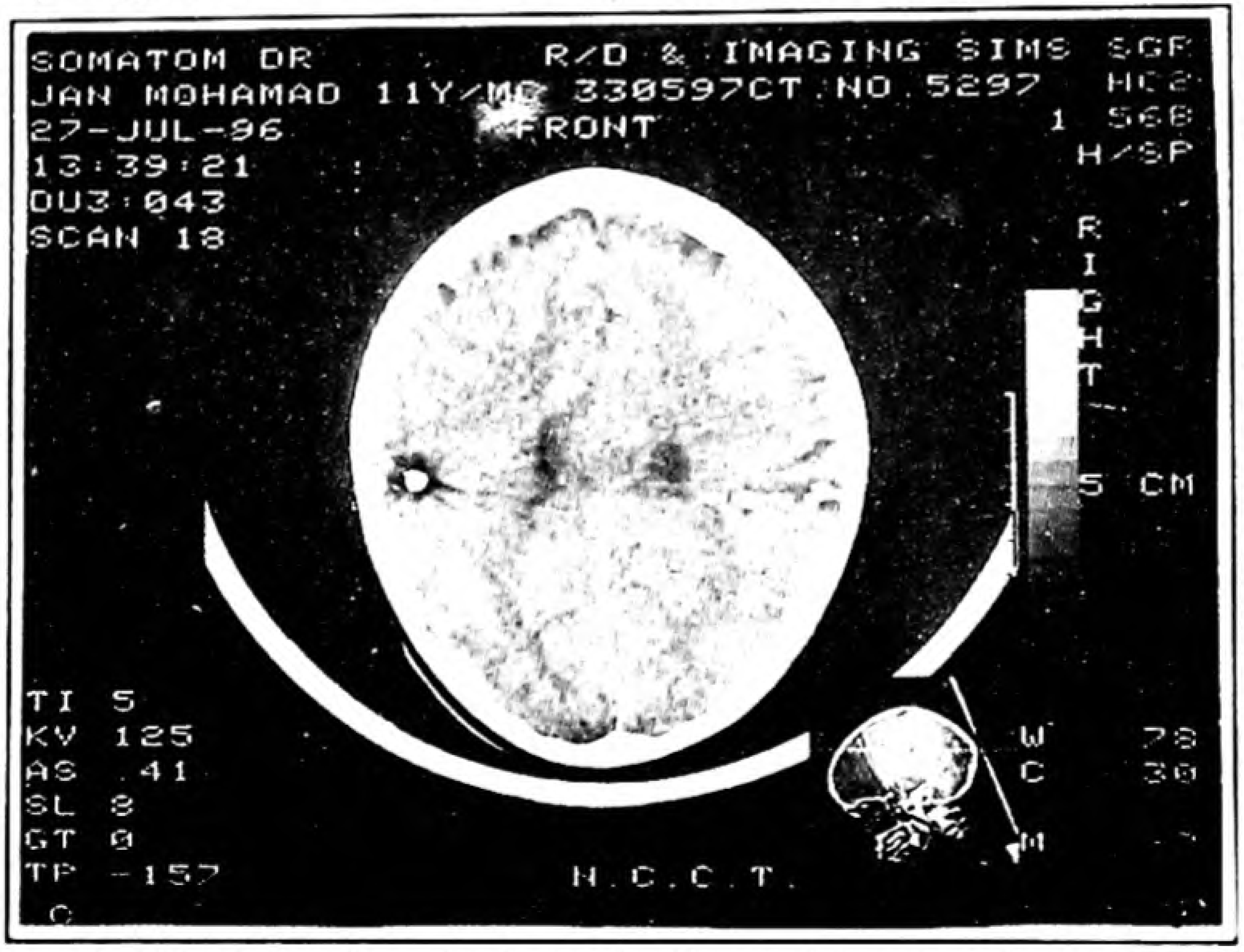
Surgical debridement of the wound was done. Necrotic scalp, muscle and brain tissue was removed. Contaminated indriven bone fragments and foreign bodies were removed. Haematomas and contused brain presenting as mass lesions were evacuated. Bullet track was followed to its site. Proper haemostasis was achieved. Dural and scalp closure was done meticulously.



Lateral X-ray Skull showing bullet in parietal region

Post operatively patients were shifted to intensive care unit. Intracranial pressure was monitored and patients were treated by hyperventilation and decongestant therapy. All patients received broad spectrum antibiotics, analgesics and prophylactic anticonvulsive therapy. Outcome was evaluated by Glasgow outcome scale.

Repeat postoperative check CT scan was done within first week after operation and at the time of discharge. Stitches were removed on 10th post operative day.



CT Head showing missile tract with a pellet on the otherside

Results

70 patients were directly admitted to A&E department of our hospital, while as the rest 24 patients were referred from other hospitals. There were 72 male patients and 22 female patients. Youngest patient was a 11 year old boy. Most patients were young adults (35-45 yrs.).

11 patients died in the casuality or in the emergency operation theatre even after being given all resuscitative measures. 33 patients had received injuries from shell fragments flying from explosive devices and rest had firearm injuries.

Neurological evaluation after resuscitation revealed that 55 patients had a GCS of 3-5; 6 had GCS of 6 to 8; 10 had GCS of 9 to 12; and 23 presented with a GCS score of 13 to 15.

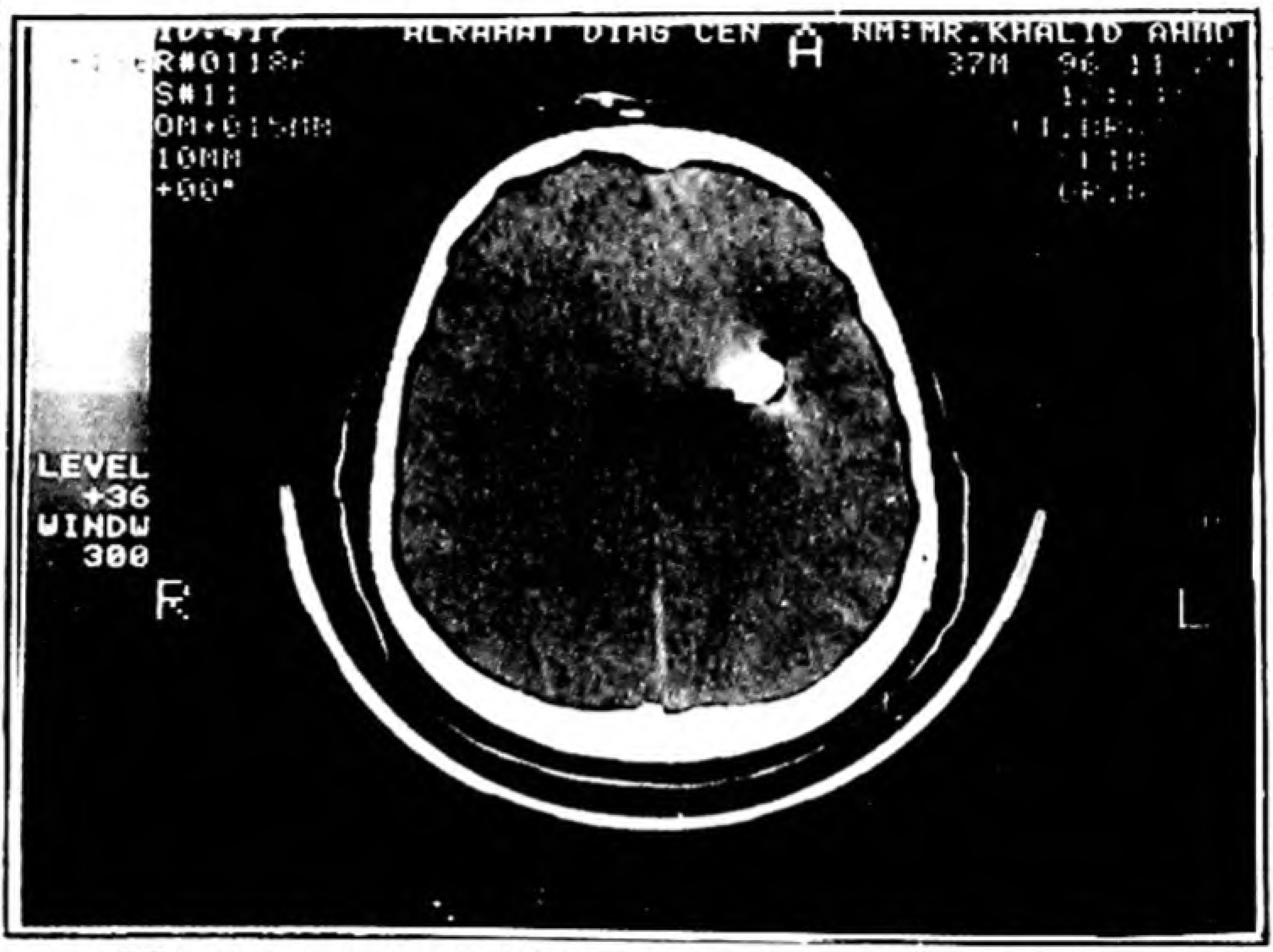
CT scan of head was done on all 83 patients except the ones who died in casuality. Only 66 patients were operated.

Glasgow outcome scale results showed that 55 patients died; 5 were left in a permanent vegetative state, 6 were severely disabled, 12 were moderately disabled and 16 had good outcome at discharge.

Operative mortality for this series was approximately 33% (22/66). 12 patients developed postoperative CSF leak and meningitis and were managed conservatively. 3 patients developed brain abscess and required formal cranitomy and evacuation of brain abscess. 11 patients had severe wound infection and wound dehiscence, which required control of wound infection and secondary suturing of the wound. One patient died of DIC following massive transfusion and two patients died of severe bronchopneumonia following aspiration pneumonititis.

Discussion

In the management of patients with penetrating injuries of head, immediate resuscitation at the site of injuryand early transportation to a neurosurgical centre is very important. This prevents secondary complications like hypoxia and hypotension. Similar observations were found to yield better results in our series and also by Kaufmann et al[12] and Grahm et al[10].



CT Head showing bullet fragment with surrounding edema

Inspite of aggressive resuscitation many patients died either in accident and emergency department or before any surgical intervention could be carried out, as the general condition of such patients would be very bad. Patients with low GCS scale of 3 to 5 had poor outcome, whether or not surgery was performed on them. Kaufmann et al however reported that 3 of 86 patients with GCS scores of 3 to 5 survived with satisfactory outcome.

We used GCS score to predict outcome of the patients. 55 patients with a GCS of 3 to 5 had very poor outcome, out of 20 patients from this group, who were operated, only 5 patients lived, but were left with sever neurodeficit postoperatively.

Patients with GCS score to 9 to 12 and 13 to 15 had good outcome. Similar observations were made by Graham et al.

Plain x-ray of the skull was done in all patients admitted to the hospital. X-rays showed fractures of the skull; and presence of bullet or shell fragments in the head.

Computed tomography was the investigation of choice and was performed in all patients who improved after resuscitation. CT scan demonstrates the extent of injury, the entire tract of the missile injury, size and site of associated contusion and haematomas, and presence of any foreign body in the brain. CT findings were also used to prognosticate the outcome of patients. Nagil et al[13] and Ghram et al found that patient with bihemispheric injuries and intraventricular haemorrhages had poor outcome. In our series none of the 6 patients with such type of brain injuries lived.

The aim was to perform an early and adequate surgical debridement of the necrotic tissue. Grahm et al are of the opinion that early surgical intervention reduced both the incidence of increased intracranial pressure and the infection rate. During World War I in 1917 Harwey Cushings[14] reduced the mortality in 229 patients to 29% by performing early treatment. Importance of quick debridement was again emphasized by Martin and Campbell[15] during World War II, who found a mortality of only 3.7% in 426 patients. Similar low mortality was reported by Hammon[6] from the Vietnam experience of 9.7% in 2, 187 patients. More recently Aarabi[16] reported a mortality of 8.8% in 125 patients, treated during Iran-Iraq conflict.

Even though major predictors of survival have been level of consciousness, intracranial haematomas, ventricular injury and bihemispheric injury, early surgical intervention might salvage some patients otherwise considered hopeless.[13,17]

Glasgow outcome scale (GOS) scoring as described by Jennett and Bond[18] were used. In our series GOS score revealed following results.

GOS	1 -	Death	55
	2 -	Persistent vegetative state	05
	3 -	Severe disability	06
	4 -	Moderate disability	12
	5 -	Good recovery	16

Late surgical intervention is associated with development of postoperative brain infections. 2 patients in our series developed brain abscess and 4 patients had meningitis following postoperative CSF leak.

Patients who have survived are on our follow-up. They are attending our OPD clinic after every two weeks. The patients belonging to GOS grade 5 have been attending to their duties regularly. They are performing routine day to day work.

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Pattern of Thyroid Lesions By Fine Needle Aspiration Cytology in Kashmir

Mohan Lal Bhat M.D.; Rashida Parveen Chishti. M.D.; Mansoor Ahmad Laharwal M.B.B.S.

***Abstract** : 250 cases of thyroid lesions were studied by fine needle aspiration cytology over a period of three years. Of these 234 were benign lesions, which included 59 males and 175 females. The total number of malignant lesions was 16, which included 1 males and 12 females. The preponderance of both types of lesions was observed in females as compared to males.*

***Key words:** Adenoma, Carcinoma, FNAC, Thyroid lesions.*

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Introduction

Thyroid swellings are commonly encountered in the clinical practice in this part of the country, particularly so in the hill terrains of Kashmir valley. The different types of thyroid lesions which lead to thyroid swellings were evaluated by Fine Needle Aspiration Cytology in a total of 250 patients over a period of three years. Therefore, the present study is being presented to highlight the incidence of thyroid lesions with respect to the microscopic examination of the smears obtained as well as age and sex distribution. These cases were diagnosed by FNAC only.

Material and Methods:

The study was conducted in the cytology section of the Pathology department of Govt. Medical College, Srinagar. The patients were sent to the teaching hospitals attached to the Govt. Medical College, Srinagar. The study was conducted from January 1993 to December 1995, which included 250 cases. FNAC was performed using conventional methods and the smears stained with May Grunwald Geisma (MCG) stain. In 35 cases, aspiration did not yield any cellular material and hence aspiration was repeated in these cases.

Results:

In the present study, the age of patients ranged from 3 years to 75 years. There were 187 females and 63 males. Females out-numbered males in both benign and malignant lesions. The most common age group involved among females was 21-30 years, followed by the age group 31-40 years and the least common was 71-80 years. Among males the most common age group involved was 41-50 years followed by the age group of 21-30 years and the least common was 71-80 years. Of the total of 250 cases 63 cases (25.2%) were males whereas 187 cases (74.8%) were females. The results are summarised in Table (1).

The results obtained by FNAC of different types of thyroid lesions in different age groups are summarised in Table (2). Of the 250 cases, 234 cases (93.6%) were benign lesions of which 87 (34.8%) were colloid goitres, 81 cases (32.4%) were colloid adenomas, 40 cases (16%) were follicular adenomas, 17 cases (6.8%) were thyroid included subacute as well as granulomatous types and the remaining 2 cases (0.8%), which yielded pus like material on aspiration and showed necrotic material on microscopic examination, were grouped as simple abscesses. A total of 16 cases (6.4%) of malignant lesions were encountered which included 10 cases (4%) of papillary carcinoma of thyroid and 6 cases (2.4%) of follicular carcinoma of thyroid. Out of a total of 16 cases of malignant thyroid lesions, 4 cases (1.6%) were

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Table (1)

Showing age and sex distribution of Benign and Malignant Thyroid lesions

Age In Years	Benign Lesion		Malignant Lesions		Total No. of cases
	Males	Females	Males	Females	
1-10	6(2.4%)	4(1.6%)	-	-	10(4%)
11-20	6(2.4%)	26(10.4%)	-	-	32(12.8%)
21-30	9(3.6%)	38(15.2%)	1(0.4%)	2(0.8%)	50(20%)
31-40	8(3.2%)	34(13.2%)	1(0.4%)	3(1.2%)	46(18.4%)
41-50	11(4.4%)	29(11.6%)	1(0.4%)	3(1.2%)	44(17.6%)
51-60	6(2.4%)	23(9.2%)	-	3(1.2%)	32(12.8%)
61-70	3(1.2%)	9(3.6%)	-	1(0.4%)	13(5.2%)
71-80	1(0.4%)	-	-	-	1(0.4%)
Not known	9(3.6%)	12(4.8%)	1(0.4%)	-	22(8.8%)
Total	59(23.6%)	175(70%)	4(1.6%)	12(4.8%)	250

Table (2)

Showing pattern of thyroid lesions in different age groups

Thyroid Lesion	Age Groups									Total No. of cases
	1-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	Not Known	
Benign										
1. Colloid Goitre	3	17	14	14	15	10	8	1	5	87(34.8%)
2. Adenomas										
a:- Colloid	-	7	18	17	16	13	2	-	8	81(32.4%)
b:- Follicular	1	4	13	4	6	5	-	-	7	40(16%)
c:- Papillary	-	-	-	-	-	-	-	-	-	
3. Cysts	5	4	1	5	1	1	-	-	-	17 (6.8%)
4. Thyroiditis	-	-	1	2	1	-	2	-	1	7(2.8%)
5. Abscesses	1	-	-	-	1	-	-	-	-	2(0.8%)
Malignant										
1. Papillary	-	-	2	4	1	1	1	-	1	10(4%)
2. Follicular	-	-	1	1	2	2	-	-	-	6(2.4%)

males whereas 12 cases (4.8%) were females. A small group, of which the age was not knuown and had both benign as well as malignant lesions, constituted 22 cases (8.8%).

Discussion

Fine Needle Aspiration Cytology has proved to be more popular in recent years because of its great convenience and accuracy in the diagnosis of thyroid lesions. In the Kashmir valley the commonest cause of thyroid enlargement, which has been observed in the present study is colloid goitre (34.8%). In a similar study by Bhaskaran et al (1990).[2] 16 cases of colloid goitre out of a total of 258 cases (6.2%) have been reported. The possible reason for a higher percentage of colloid goitres in our study is a iack of Iodine in the sub-himalayan region of Kashmir, particularly in the hilly terrain.

In the present study, a total of 121 cases (48.4%) of adenomas, which included 81 cases (32.4%) of colloid adenomas and 40 cases (16%) of follicular adenomas[3] were diagnosed on fine aspiration cytology. No papillary adenoma was observed in this study. Colloid adenomas were the second common cause of thyroid enlargement in Kashmir. In a similar study, Coute et al (1994)[4] have reported 34 cases of adenomatous goitres out of a total of 137 cases of thyroid lesion thus making a total percentage of 24.8. Our study shows a slightly higher incidence of the lesion.

17 cases (7.2%) were diagnosed as cystic lesions[5] which included 10 cases of thyroglossal cysts and 7 cases of simple cysts of thyroid and 7 cases (2.9%) as thyroiditis,[6] which included subacute as well as granulomatous types. 2 cases (0.8%) of simple thyroid abscesses were also observed in this study.

Amongst the malignant lesions,[7] papillary carcinoma was the most common and was observed in 10 cases (4%) whereas follicular carcinoma was found in 6 cases (2.4%). Females outnumbered the males in incidence of malignant lesions as observed in the present study. The present study confirms the value of FNAC in diagnosing the different types of thyroid lesions with high accuracy.[8] The potential ability lies in detecting malignant lesions with high accuracy.

Conclusion:

FNAC, the cheapest, easiest and a non-traumatable method of diagnosis in our poor patients admitted in the Govt. hospitals need not be overemphasised. From the present study it is concluded that the microscopic examination of the material obtained on fine needle aspiration cytology of thyroid is an effective method in diagnosing and categorising the different types of thyroid lesions in Kashmir and has an accuracy of nearly 90%.

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Intraocular Lens Implantation In Traumatic Cataract

Bashir Ahmad MS; FICS; Shamim Sadiq MBBS; Amarjeet Singh MS.

***Abstract** : The present study was conducted in 50 cases of traumatic cataract, undergoing posterior chamber intraocular lens implantation, and followed for 6 months. 76% patients were male and 24% female. Associated findings were Adherant leucoma 24%, Posterior synechiae 23%, Distorted pupil 26%. The common postoperative complication were seen as striate keratitis 10%, Corneal edema 6%, Iris pigment deposits 12%, Uveitis 26%. Pupil capture 32%, Decentration 2%, Pupillary membrane formation 3%, and posterior capsular opacification 22%. The final visual acutiy was seen as 6/6-6/9 in 10%, 6/12-6/18 in 40%, 6/24-6/36 in 36%, 6/60 or less in 2%, and not recordable in 10%. It was concluded that proper aspiration of lens matter with posterior chamber intraocular lens implantation is safe and effective method of treatment in uniocular traumatic cataract.*

Key words: Traumatic cataract, posterior chamber, IOL, Uveitis, Pupil capture, Posterior capsular opacification.

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Penetrating injuries being quite common, and lens is the most commonly injred structure, which can lead to decrease in visual acuity. To restore normal visual acuity the catracteous lens must be removed. Most of the time the injury being unilateral, the biocular vision after surgery can only be attained by either a contact lens or intraocular lens. The posterior chamber intraocular lens is method of choice for restoration of visual acuity in such cases.

The present study was undertaken to study the post-operative complications after posterior chamber intraocular lens implantation in cases with traumatic cataract.

Material and Methods:

In this series 50 cases of traumatic cataract, under going lens aspiration with posterior chamber IOL implantation were studied and followed up for 6 months.

Patients were preoperatively examined by diffuse light and slit lamp, preperative intraocular pressure and visual acuity was recorded. All other associated findings with cataract were noted down and surgical plan was decided depending upon the associated complication which was as;

1. Anterior capsulotomy, lens aspiration, posterior chamber IOL implantation.
2. Anterior capsulotomy, lens aspiration, anterior vitrectomy, posterior chamber IOL implantation.
3. Synechiotomy, anterior capsulotomy posterior chamber IOL implantation.
4. Secondary posterior chamber IOL implantation.

Viscoelastic material in the form of 2% methylcellulose was used in all cases.

Sub-conjunctival steroid-antibiotic was given at the conclusion of surgery.

Postoperatively, patients were examined by slit lamp on Ist day, 2nd day, 4th day and after 1 week, then weekly for one month and then but nightly for 6 months, after which final results were drawn. The complications were noted down and managed accordingly.

Results:

Out of 50 cases of traumatic cataract, 38(76%) were males and 12(24%) females. The youngest patient taken up for the study was of 8 years old and oldest 50 years, with mean age of 20.40+10.95 years. The most common mode of injury was found to be stick, followed by knife, stone and other miscellaneous articles. The associated findings in addition to traumatic cataract were found to be corneal opacity (60%), adherant leukoma 24%, posterior synechiae 28%, Torn/distorted pupil 26%. Intraoperative findings during surgery were posterior

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synechiae 28%, posterior capsular rebt 10%, posterior capsular opacification 8%, positive vitreous pressure 4% and torn/distorted pupils 26%, 20% cased did not show any other findings except traumatic cataract Postoperative findings, immediately after surgery were seen as:

Table I

Findings	No. of cases	%age
1. Striate keratitis	5	10%
2. Corneal edema	3	6%
3. Iris pigment dispersion	6	12%
4. Uveitis	13	26%

In immediate postoperative period striate keratitis was seen in 5 cases which was treated with steroid drops, corneal edema also resolved with topical steroid drops. In these patients intraocular pressure was normal, iris pigment deposit was seen in 12% of cases. The incidence of uveitis was seen to be in 26% which was treated with topical and subconjunctival steroids, and responded to treatment.

Of the delayed postoperative findings that were seen 16 cases (32%) developed pupil capture, no treatment was done. 3 cases (6%), developed an opaque membrane in pupillary area which required surgical intervention.

Posterior capsular opacification was seen in 11(22%) cases out of which 5 cases (10%), showed loss of visual acuity due to it and required surgical intervention.

2 cases (4%), showed decentration of lens, with appearance of sunset syndrome.

5 patients (10%), showed visual acuity of 6/6 to 6/9, 20 patients (40%), showed visual acuity of 6/12-6/18, 18 patients (36%), showed visual acuity of 6/24-6/36 while as 2 patients showed visual acuity 6/60 or less, and in 5(10%), visual acuity could not be recorded due to non-coperation of patients.

The reasons for poor visual acuity were corneal opacities, posterior capsular opacification.

Discussion

The incidence of striate keratitis in present study ws 10%, while as Pasricha[10] (1990), reported this incidence as 16.6%, which is more than present study and Ashish Deb[2] (1990), reported as 12.5%, which as Gupta etal[6] (1990) reported incidence as 6% which is less than present study. Corneal edema in present study was 6%, while as David Hiles[5] (1984), reported 17.4% which is quite higher than this study. Iris pigment and IOL was seen in 12% while as Alaxander TA[1] (1987), reporterd 47.8% which is quite high. Uveitis reported in present study was 26%, which is quite as Nitin Verma[9] et al (1991), 24% Pasricha[10] (1990), 24% Ashish Deb[2] (1990) 25%, which are quite close to our study and Gupta et al[7] (1992, 81.8% and Burke[3] (1987), 35% which are higher than present study.

Pupil capture was seen in 32% in this study, while as Dada et al[4] (1990), reported 16%, Subir Sen[12] (1990), 14% Ashish Deb[2] (1990), 12.5%, and Alaxander TA[1] (1987), and Gupta et al[7] (1992) 9%, which is quite low than our study.

Decentration was seen in 4%, cases, while as Kamlesh[8] et al (1991), repoted 3.3% which is quite close to present study while as Subir Sen[12] (1990), repotred 6.8%, Alaxander[1] (1987), 6.5%, Gupta[7] et al (1992), reported 9% which is higher than present study. Pupillary memberane formation was seen in 6% cases, while as Dada et al[4] (1990), Which is less reported 4% which is less than present study.

Posterior capsular opacification was seen in 22% of cases while as Singh et al[11] (1990), reported 76% and Pasricha[10] (1971), 13.8% which is quite less than present study while as Burke[3] et al (1990), repoted 30%, Subir Sen[12] (1990) 33.9% and Alexander[1] et al (1987). 34.8% which is quite higher than present study.

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Comparative study of spinal anaesthesia with Xylocaine alone and Xylocaine with low dose Ketamine

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***Absract** : Fifty adult male patients undergoing different types of routine surgery below umbilicus subjected to spinal anaesthesia were divided into two groups of 25 patients each. Group I was given xylocaine 5% (2 ml) and Group II was given Xylocaine 5% (1.5ml) plus Ketamine 3 mgs (0.5ml). The onset and duration of action of analgesia and motor block, pulse rate and changes in blood pressure as well as side effects were studied. The mean duration of analgesia was 94.48±4.12 mts in group I and 99.78±6.82 mts in group II which was statistically significant (p<0.005). The mean duration of motor block in group I and group II was 82.56±5.09 mts and 105.40±10.89 minutes respectively which was statiscally highly significant (p<.0.001). Group II had the advantage of cardiovascular stability and was without any other side effects.*

Key words: Intrathecal, Xylocaine, Ketamine, Analgesia, Motor blockade.

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Introduction

Improvements have been made in the drugs and their combinations used for subarachnoid block to prolong duration of anaesthesia and painfree post operative period. Use of intrathecal narcotics with or without local anaesthetic agents is a step forward to achieve this goal. Narcotics are effective analgesics but have a major disadvantage of respiratory depression. In a quest for an ideal drug to be used intrathecally for analgesia, Brock, Utne and associates (1982)[1] conducted several animal studies about the effects of Ketamine on spinal cord. Ahuja (1983)[2] and Carasco et al (1984)[3] confirmed the compatibility of Ketamine and spinal neural tissue and reported adequate analgesia after its intrathecal use.

The present study has evaluated the effectiveness of lignocaine hydrochloride alone and its combination with low dose Ketamine hydrochloride for the use of producing effective subarachnoid block. Ketamine is of special interest as very little data is available on its intrathecal use in humans, though animal experiments have adequately proven its non-toxicity to neural tissue of spinal cord.

Material and Methods

50 male patients in the age group of 25 to 65 years belonging to ASA class I and II, posted for lower abdominal, perineal and lower limb surgical procedures were studied. The patients were divided into two groups I and II of 25 patients each. The patients were allocated to the modalities of anaesthesia on random basis.

Group I patients received intrathecal 5% hyperbaric xylocaine (2ml) and it acted as control group. In group II, patients received intrathecal hyperbaric xylocaine 5% (1.5ml) plus ketamine hydrochloride 5mg (0.5ml) making a total volume of 2ml. No premedication was used. Monitoring equipment was used to monitor continuous ECG, blood pressure and oxygen saturation.

Patients were given subarachnoid block at L_3-L_4 interspace using 22 guage spinal needle in lateral position. Patients were turned to supine position immediately with headup tilt 15-20°. The time of onset, duration of analgesia, motor block, and complications, if any, were observed. Mean arterial blood pressure (MABP) and heart rate were recorded every 10 minutes.

Results were analysed by using students 't' test.

Result

The age and weight distribution in both the groups were comparable. The onset of analgesia in group I and group II was 2.65±0.48 mts and 3.0±0.76 mts.

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respectively. The discrepancy in the average onset of analgesia between the two groups was statistically insignificant. The duration of analgesia was 94.48±4.12 mts and 99.78±6.82 mts. in group I & group II respectively which was statistically significant (p<.005). The onset of motor blockade in group I was 6.28±0.61 mts and in group II was 7.76±1.09 mts. The discrepancy in the average onset of motor blockade between the two groups was statistically highly significant (p<.001) as shown in table I. The duration of motor blockage in group I and group II was 82.56±5.09 mts and 105.40±10.89 mts respectively as indicated in table.II. The comparison between the two groups was statistically highly significant (p<.001).

Table I
Onset and duration of motor block (Minutes)

Motor block	Group I	Group II	t	p	Remarks
Onset (mts) Mean± SD	6.28±0.61	7.76±1.09	5.92	<.001	HS
Duration (mts) Mean±SD	82.56±5.09	105.40±10.89	9.60	<.001	HS

There was a statistically highly significant (p<.001) fall in heart rate at 20,30.40, and 50 minutes of study and statistically significant fall (p<.005) at 10,60 ad 70 minutes of the study in group I when compared with base line value. The change in heart rate from base line value was statistically insignificant in group II. The discrepancy in the mean heart rate in group I as compared to group II was statistically significant at 20,30,70 and 80 minutes of the study as shown in table II.

Table II
Mean heart rate

Time(mts)	Mean±SD Group I	Group II	t	p	Remarks
Pre-block	84.36±6.13	80.80±7.39	1.87	>.05	NS
0 mts	84.20±5.90	81.64±7.22	1.92	>.05	NS
10 mts	75.96±8.15	81.20±6.58	2.53	<.025	Significant
20 mts	76.04±8.08	81.08±6.54	2.45	<.025	Significant
30 mts	78.12±6.33	80.56±6.48	1.36	>.10	NS
40 mts	80.44±6.11	80.08±6.68	0.20	>.05	NS
50 mts	82.80±6.02	80.00±6.32	1.62	>.10	NS
60 mts	82.12±6.97	82.60±6.80	0.42	>.05	NS
70 mts	83.80±6.03	79.98±6.12	2.25	<.05	Sig
80 mts	83.56±6.03	79.00±6.07	2.70	<.01	Sig

The decrease in mean arterial blood pressure as compared to base line in group I was statistically significant (p<.025) at 10 mts and statistically significant (p<.025) at 10 mts and statistically highly significant (p<.001) at all the instances from 20 to 80 minutes of study. The decrease in mean arterial pressure in group II at all the instances of the study was statistically insignificant as compared to base line value. The difference in mean arterial blood pressure observed in group I as compared to group I was statistically highly significant (p<.001) at 10,20 and 70 and statistically significant (p<.01) at 30,40,60 and 80 minutes of study. The incidence of complications revealed that nausea and vomiting occurred in 8% (n=2) and headache in 8% (n=2) patients in group I. No complications occured in group II patients.

Discussion

It is essential to understand the variations in the advantages and problems to various drugs used for spinal analgesia to select the effective and safe drug for a particular purpose. It is a common practice to use additives to local anaesthetics in spinal anaesthesia,

Ketamine in small doses were given epidurally to treat intractable cancer pain[4]. Bion in 1984 used ketamine to produce an effective subarachanoid block. He found, ketamine when given intrathecally produced sensory block only and no motor paralysis. The mean duration of effective block was 60 minutes only[5]. Kumar (1986) used 5mgs ketamine with 1.5 ml of lignocaine 5% and overcame the disadvantages of short duration in Bion's study[6].

In the present study intrathecal hyperbaric xylocaine hydrochloride was compared with a combination of ketamine (5mg) and hyperbaric xylocaine hydrochloride chloride for analgesia, motor blockade and hemodynamic profile Mean duration of analgesia in group II was more than in Group I. The duration of motor block was prolonged in group II as compared to group I which was satistically highly significant (p<.001). Our results of relatively better hemodynamic stability in group II were in accordance with the study by Bion JF[5] who observed same results.

Our results of incidence of nausea and vomiting in group I was in accordance with the results of the study conducted by Damle Nalini et al (1990)[7]. No patient in group II had any complication which was contradictory to the results of the study conducted by Kumar P (1986)[6] in which 16.5% of patients had headache and

8.3% had retention of urine.

The suggested mechanisms involved in the action of intrathecal ketamine hydrochloride include production of lamina-specific inhibition of dorsal horn unit activity, agonism with opiate receptors[8]. Ketamine potentiates the effect of 5HT and nor-adrenaline by inhibiting uptake[9]. Ketamine has been observed to selectively suppress lamina I and lamine V. Ketamine acts on NMDA receptors which may effect synthesis or release of nitric oxide[10,11].

So it is concluded that ketamine hydrochloride can be combined with hyperbaric xylocaine to provide adequate analgesia and prolong the duration of motor blockade. This combination also provides better hemodynamic stability with less side effects.

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CASE REPORTS

Pulmonary Hypertension: An Unusual Presentation of Alveolar Cell Carcinoma of the Lung

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Abstract: Lung cancer is the leading cause of cancer-related deaths in the USA, with an estimated 178,100 new cases in 1997, accounting for 13% of cancer diagnoses. The incidence rate is declining in men, from a high of 87 per 100,000 in 1984 to 77 in 1993. Recently the rate of increase among women has begun to show; however, since 1987, more women have died of lung cancer, which, for over 40 years, was the major cause of cancer death in women. In 1993, the incidence rate in women was 42 per 100,000[1]. The common well-known presentations of lung cancer are often caused by airway obstruction - cough, sputum production, hemoptysis, unresolved pneumonias, etc, and invasion of neighboring and/or distant organs with metastasis. Lung cancer, commonly, is not associated with gas exchange problems. We report a patient with lung cancer of Bronchoalveolar type, whose major clinical presentation resulted from severe hypoxia, hypercapnia leading to pulmonary hypertension, cor pulmonale, right-heart failure and eventually death.

Keywords : Alveolar cell carcinoma, pulmonary hypertension.

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Case Report

A 56 year-old man was hospitalized in July 1969 for shortness of breath. His illness had started six months earlier with edema of the legs, and persistent cough with copious amounts of clear sputum. Chest x-ray showed a homogenous density in the right upper lobe. An open-lung biopsy revealed minimal interstitial fibrosis. Sputum cytology and bronchial washing were negative for tumor cells. A hemogram revealed Hb 17.5 and WBC 11,000. The patient was discharged on 60mg of Prednisolone daily.

He continued to have shortness of breath, edema, and productive cough, and after six months was readmitted in December 1969. On examination he had cyanosis and was plethoric, with a respiratory rate of 26/min. The neck veins were distended, a left parasternal heave was palpated, and P2 was accentuated. There was 3+ pitting edema of the legs, and the fingers were clubbed and cyanotic.

Laboratory data revealed Hb 19.6, Hct 62, WBC 10,800. Arterial blood gases (ABG) on room air showed pH 7.38, $PaCO_2$ 50mm Hg, PO2 31mm Hg. EKG revealed a right axis deviation with peaked P waves in lead 2 and tall R waves in lead V_1. Chest x-ray showed a homogenous density involving the entire right hemithorax and the lower third of the left hemithorax (fig. 1). Sputum cytology showed atypical bronchial mucosal cells.

The patient was treated with digitalis, phlebotomy and oxygen. On 28% Oxygen, his pH was 7.30, $PaCO_2$ 70mm Hg, PO_2 45mm Hg, and Sao_2 75%. He died suddenly on the seventh hospital day.

At autopsy, diffuse and multinodular bronchiolar cell carcinoma was found, involving both lungs, with metastasis to peribronchial lymph nodes. There was no extrathoracic spread of the tumor, nor was there any evidence of direct invasion of pulmonary capillaries by the tumor.

Discussion

Bronchoalveolar carcinoma, a special subtype of Adenocarcinoma, accounts for 1-5% of the primary lung tumors. It may be localized, presenting as a nodule (60%), or may be diffuse "pneumonic", presenting as pulmonary infiltrate or area of lobar consolidation mimicking infection as in the patient mentioned. The

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diffuse form has a worse prognosis, and has been associated with chronic inflammation of the lung, such as interstitial fibrosis and areas of scarring. This form is distinguished by the relative preservation of the lung parenchyma, which acts as a support or scaffolding for the growth of the tumor cells, "lepidic growth". These tumors grow in a single layer, along the intact walls of the terminal airways and alveoli, in some areas filling the alveolar spaces.

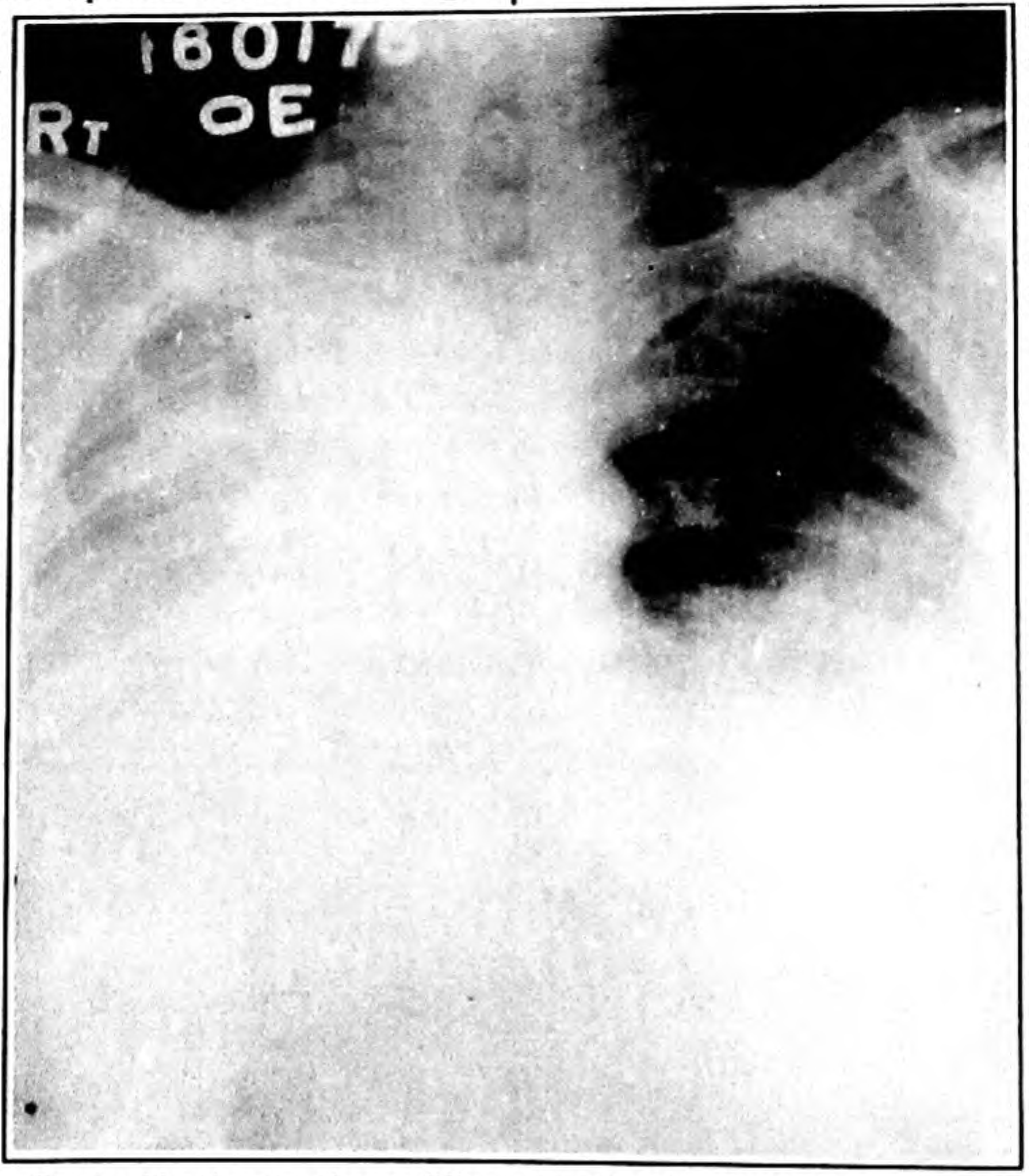

Fig.1 : Chest x-ray shows diffuse opacification of right hemithorax and lower third of left hemithorax

Radiographically bronchoalveolar carcinoma may present as a poorly defined but extensive parenchymal mass. Lepidic form of growth may be facilitated by aspiration route, in addition to the commonly encountered hematogenous and lymphatic metastasis. Thus, the tumor may reach an enormous size but the bronchioles remain preserved. Thus, pulmonary ventilation scans in such patients fail to show any abnormality. Due to the relative preservation of the lung architecture, there is not much interference with the capillary perfusion. As a result, the lung perfusion scans also fail to show any abnormality, indicating that the regional perfusion is intact. Thus an essentially normal lung ventilation and perfusion scan, with a radiograph demonstrating extensive infiltration, should give rise to suspicion of this form of cancer.[2]

Our patient presented with symptoms and signs of right-heart failure. This is a very rare manifestation of lung cancer; a single case has been reported previously in which the mechanism was due to direct invasion by the tumor cells of the capillaries[3], a finding not seen in our patient.

In our patient, secondary mechanisms due to extensive tumor involvement seem to have played a major role in the development of severe pulmonary hypertension, culminating in right-sided heart failure. These mechanisms are especially of significance and have a cumulative effect when they involve a large lung volume. This patient had involvement of the entire right hemithorax and the left lower third of the left hemithorax, as evidenced on chest x-ray.

He had raised alveolar-arterial oxygen gradient, in addition to the hypercapnia. The lepidic form of growth of adenocarcinoma impairs efficient gas exchange with an increase of dead space, resulting in massive right-left shunting, thus increasing the work load of the right ventricle. The result is hypoxemia and, in the more severe case, hypercapnia. Patients may present with life threatening hypoxia, and this may be graver than the underlying carcinoma itself[4]. Another proposed mechanism for the large venoarterial shunt is obstruction of the bronchioles, at and beyond the site of tumor location, by the copious mucus production by the tumor. This results in hypercapnia and hyperventilation as was seen in our patient[5].

Hypoxia acts as a local chemical vasopressor; its effect is further augmented by acidosis. Hypercapnia is also a local vasoconstrictor due to the acidosis it generates. At first these changes are reversible, but with chronicity the arterial media undergoes hypertrophy with resultant pulmonary hypertension. The resultant elevation in pulmonary artery pressure produces a significant stress on the right ventricle, which is compounded when the patient is hypoxic, as was the case in this patient.

The chronic hypoxia results in secondary erythropoiesis with a rise in the hematocrit. Adenocarcinoma can result in polycythemia due to autonomous production of erythropoietin. Although erythropoietin levels were not measured in our patient, this may have been an additive factor for the high hematocrit level (Hct 62) observed. This causes an increase in the blood viscosity producing a further elevation of right ventricular pressure.

Lastly, the tumor directly disrupts the normal pulmonary microvasculature, resulting in an increase in the afterload of the heart.

Bronchoalveolar carcinoma usually begins as a peripheral lesion, and symptoms are referable to invasion of the adjacent structures. It is also occasionally associated with the production of copious amounts of watery sputum (bronchorrhea), as was observed in our patient. This is a rare but serious problem, and is specific for this form of cancer. The sputum has similar composition as serum, and this is why it may lead to a dangerously high loss of electrolytes and fluid, sometimes resulting in serious dehydration and pre-renal azotemia. It is speculated that the sputum is produced by the tumor cells growing along the alveolar walls[6].

Clinical Pearls

1. Bronchoalveolar carcinoma may present with severe gas-exchange problems, resulting in pulmonary hypertension, cor pulmonale and right-heart failure.
2. A normal perfusion lung scan, in the presence of extensive radiographic abnormalities, is a good clinical clue for the presence of bronchoalveolar carcinoma.
3. Some patients with bronchoalveolar carcinoma have severe bronchorrhea, which can lead to serious electrolyte disturbances and salt depletion[5].
4. Bronchoalveolar carcinoma may spread within the lungs, by transbronchial aerosol mechanism.

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Survival In a Case of Severe Myocarditis with Pulmonary Oedema After Scorpion Sting

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***Abstract** : We report a case of rare survival of a young man who developed severe pulmonary oedema due to acute myocarditis and severe left ventricular dysfunction. He received early ventilatory and inotropic support, diuretics, nitrates, ACE inhibitors and steroids. He made remarkable recovery both clinically and echocardiographically.*

Key Words: Myocarditis, Pulmonary Oedema, Scorpion Sting.

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Intorduction

Scorpions are widely distributed in the Kingdom of Saudi Arabia. Many dangerous species have been described.[1]

Most fatalities are related to cardiovascular complications. Scorpion venom is a strong stimulant of sympathetic nervous system leading to tachycardia, hypertension, anxiety, diaphoresis and pulmonary edema. Some patients develop shock with peripheral vascular failure. Most deaths are due to pulmonary edema, related with acute myocarditis and severe left ventricular dysfunctions.[2,3,4] Generally, poor prognosis has been seen in our hospital and elsewhere after a cardiovascular collapse due to scorpion sting.[5]

This patient showed classical features of scorpion-venom induced tachycardia, initial hypertension, pulmonary oedema, acute myocarditis with left ventricular dilation and severe dysfunction. He required intensive therapeutic intervention leading to his survival and good recovery.

Case Report

This 27 year old gentleman was stung on right index finger, following that he developed pain and numbness at local site, which extended to the arm. Within two hours he developed severe breathlessness. He was rushed to a local hospital, where he was found to be in pulmonary edema with high BP of 180/110 mmHg. He was given intravenous frusemide and referred to our institution. On arrival (6 hours after the sting) he was very sick, orthopnoic, tachypnoeic and had cold peripheries. Pulse rate 110/minute, BP= 80/60 mmHg. Chest was full of crackles. Heart sounds S1 and S2 were heard. There was no neurological deficit and no bleeding manifestation. Blood gases showed hypoxia (oxygen saturatiuon = 60%). Patient was immediately intubated and ventilated with PEEP. He was given i/v frusemide, i/v/ Hydrocortisone and Antiscorpion venom.

Investigations revealed very high cardiac enzymes; CPK = 2053 u/I. AST = 97 units, LDH = 545 units. Serum amylase was elevated (240 units). Other biochemical parameters including sodium, potassium, blood sugar, calcium, phosphate and coagulation profile were within normal limits. Cardiac monitoring and electrocardiogram revealed sinus tachycardia with no conduction defects. X-ray chest showed pulmonary edema. 2-D Echo Colour Doppler studies were done serially. First echo showed global hypokinesia with LV cavity dilatation with ejection fraction of 20%.

Patient was weaned off the respirator after two days. In view of left ventricular dilatation and dysfunction he received captopril 25mg three times a day and nitrates (Isordil 10 mg TDS) in addition to i.v. and oral frusemide. Dobutamine infusion was given to maintain blood pressure. It was then tapered off when BP stayed within normal range. Patient received injection gentamicin and injection ampicillin as he developed a patch of pneumonia at left base. He also received maintenance of oral steroids.

After one week of hospitalization patient started showing signs of recovery. His pulmonary oedema cleared. Heart rate and respiratory rate settled gradually. Cardiac enzymes came down. CPK became 275 u/1 at

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one week and 20u/1 at the end of 3 weeks. Echocardiographically, he showed steady improvement of left ventricular function and reduction of left ventricular size. Ejection fraction increased to 40% at 2 weeks and 56% at the time of discharge. He showed gradual symptomatic recovery as well.

He stayed in hospital for total of 25 days, out of which 13 days were spent in Intensive & Cardiac Care Units. At the time of going home he had minimum symptoms; the steroids had been tapered off; captopril and nitrates were continued till further OPD follow up.

Discussion

Scorpion venom contains lethal cardiotoxins & neurotoxins.[6] Cardiotoxic complication are more common than neurotoxic.[7]

Scorpion venom causes massive release of catecholamines and acetylcholine. The catecholamine related alpha-stimulation produces vasconstriction causing hypertension while Beta-adreneric stimulation leads to hypotension. Other cardiovascular complications including dysrrhythmias (tachy & brady), myocarditis, bundle branch blocks, abnormal ST segments, abnormal Q&T waves. & prolonged QT interval have been described. Pulmonary oedema is a fatal complication of multifactorial origin; contributed by abnormalities of cardiac rate, rhythm, contractility and peripheral vascular resistance.[2,4,8]

On pathological examination, hearts may be grossly normal or dilated; microscopy reveals degeneration and necrosis of muscle fibres with interstitial oedema and mononuclear infiltrates. This picture is similar to that seen after catecholamine infusion in experimental animals and in patients of phaeochomocytoma.

Biochemical abnormalities like hyperglycaemia, hyper and hypokalaemia, hyper and hyponatraemia, hypercalcaemia and hyperphosphataemia have been reported. None of these were manifested in our patient.

This patient went in frank pulmonary oedema within 2 hours of the sting, associated with tachycardia and hypertension due to sympathetic system stimulation. By next 6 hours, when he reached us, he had developled hypotension with peripheral circulatory failure. He was in respiratory distress with significant hypoxaemia due to pulmonary oedema. He was salvaged with artificial ventilation and intravenous diuretics. He showed concomitant high rise of cardiac enzymes due to myocarditis.

Echocardiography demonstrated left ventriucular dilatation and disfunction with severe depression of ejection fraction. He received inotropic support with Dobutamine to improve cardiac contractility. He was also given ACE inhibitor (captopril) and Nitrates (isordil) as peripheral vasodilators. Steroids were given intravenously followed by oral Diuretics were administered as per need. He responded to this multipronged approach for supporting the myocardial function in the face of pulmonary edema. Clinical, biochemical and echocardiographic parameters showed parallel improvement.

This rare good outcome is due to his early arrival in hospital and underlying healthy heart.

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Extracranial Carotid Artery Anamolies Presenting as Ischaemic Strokes

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***Abstract** : Extracranial internal carotid artery aneurysms are uncommon but can pose serious problems, usually due to rupture or thromboembolic events. We report two young adult patients who had extracranial carotid artery anomalies in the form of abnormal loops and aneurysms, demonstrated angiographically. These were probably congenital in origin and presented as ischaemic cerebrovascular accidents or slowing of circulation at these sites.*

Key words: Extracranial internal carotid artery anomalies; ischaemic cerebrovascular accidents.

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Introduction

Extracranial aneurysms of internal carotid artery are uncommon.[1,2] Aneurysms are abnormal, localized dilatations of the blood vessels that may be of congenital, traumatic, arteriosclerotic or septic (infectious) in origin. Ionising radiation and certain connective tissue disorders are unuasual causes. Extracranial internal carotid aneurysms are principally of interest to otolaryngologists and vascular surgeons as most of them have a mass in the neck and only 15% have neurological symptoms.[3] Most of these extracranial internal carotid artery aneurysms are of congenital in origin and are confined to the level of bifurcation of common carotid artery and the proximal segment of internal carotid artery.[3] The authors present two young adult cases with extracranial carotid artery anomalies in the form of aneurysms and abnormal loops presenting as ischaemic cerebrovascular accidents.

Case Reports

Patient No. 1 Forty year old, right handed man presented with sudden onset weakness of right half of body and inability to speak, without any preceding headache, vomiting, sphincteric incontinence, convulsion, fever or head trauma. There was no history of hypertension, diabetes mellitus or smoking.

Examination revealed an asthenic patient with a pulse of 86/mt. regular and blood pressure of 130/80mmHg. Left carotid pulsations were weak as compared to the right one, with a systolic bruit heard over it. Cardiovascular system was normal. He had right sided hemiplegia and aphasia, mainly expressive. Haemogram, coagulogram, serum chemistry, lipid profile, ECG and X-ray chest were all normal. The fingings of left carotid angiogram (Fig. 1) were as under:

1. A "C" shaped abnormal loop of cervical internal carotid artery, about 2cm. wide.
2. Two aneurysms- one fusiform seen just at the distal end of the abnormal loop, another saccular one, 2 cms distal to the first aneurysm. Rest of the angiogram was normal.

Patient recovered over a period of two months on antiplatelet drugs and physiotherapy.

Patient No. 2- A 30 year old, right handed, multiparous lady admitted in the department of Neurology with the complaints of sudden onset weakness of left half of body. There was no preceding history of headache, vomiting, altered speech, unconsiousness, convulsions, fever or head trauma. There was no history of toxemia of pregnancy, hypertension or use of oral contraceptives in the past.

Examination revealed an averagely built patient with a pulse of 76/min. regular and a blood pressure of 120/80mmHg. Right carotid pulsations were weak and no bruit was heard over either carotid. Cardiovascular system, chest and abdominal examination were normal. Patient had left sided hemiplegia. There were no signs of meningeal irritation. Her haemogram, coagulogram, collagen vascular profile, serum chemistry including lipid profile were normal. Chest X-ray and ECG were normal. Right carotid angiography revealed a "ring-

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shaped loop" of cervical internal carotid artery (Fig. 2). Rest of the angiogram was normal. Patient was managed with antiplatelet drugs and physiotherapy, to which she responded well.

Discussion

Congenital aneurysms result from the maldevelopment of media, particularly at the arterial bifurcations, where the muscular coat is incomplete. Age related degenerative fragmentation of internal elastic lamina, the strongest layer of vascular wall is a contributory factor.[1] Congenital aneurysms of intracranial internal carotid artery (IC-ICA) being observed in 4% of autopsies, those of extraranial ICA are less common (L Rhorton et al, 1977; Anderson et al, 1972). The most common complications are thromboembolism, expansion, rupture and hemorrhage.

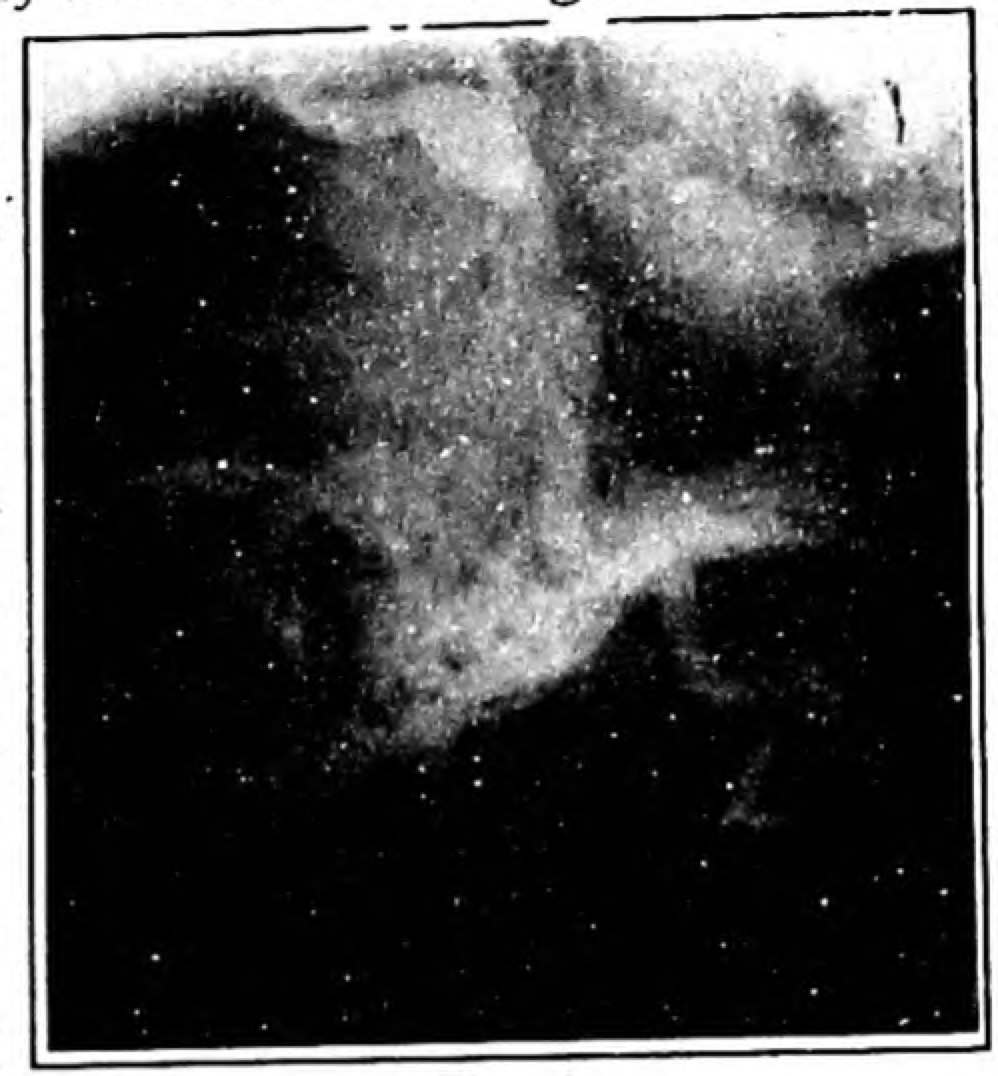

Fig - I

Thomas A Painter,[5] reported 6 cases of extracranial ICA aneurysms, out of which 4 had experienced transient cerebral ischaemia or retinal infarction and 3 had sufficient mural thrombus of atherosclerotic ulceration with the cervical carotid aneurysms. The fourth symptomatic patient had no thrombus or intimal changes, but an obvious kink at the origin of internal carotid artery from the aneurysm could have been responsible for temporary right sided hemiparesis witnessed by the referring physician.

Fig - I

Mccollumn et al, have reported only seven aneurysms of the extracranial ICA during an eleven year period when approximately 2300 operations were performed for aneurysms in other areas of the arterial tree.[3]

The causes of extracranial carotid artery aneurysms are atherosclerosis, development defects (congenital), trauma, sepsis (mycotic), irradiation for cervical malignancy, carotid artery dissection, carotid angiography and cystic medial necrosis. Other reports demonstrate a rising incidence of false aneurysms after carotid endarterectomy (McCollum et al, 1979).

In the series of twenty patients reported by Margolis and co-workers - (1972), five cases were arteriosclerotic in origin, seven were congenital, six were traumatic and two resulted from local infection. Jean Berihaya gave a detailed description of 47 cases, out of which there was one case each of internal carotid artery aneurysm due to infection, trauma, arteriosclerosis, local radiation therapy and congenital.[2,3]

The presentation in most cases is laryngological, as swelling, beneath the mandible, projection in throat, local pain, dysphagia, 9th and 11th cranial nerve palsy by stretching these nerves. Besides this, thromboembolism into the distal circulation can occur resulting in ischaemic cerebrovascular events.

The differential diagnosis of these extracranial carotid artery aneurysms include carotid body tumor, peritonsillar abscess, cervical malignancy, lymphadenopathy, or elongation and tortuosity of the cervical or subcalvian arteries (Mc Collum et al; 1979).[3]

In Jean Berihaya's description of 47 cases, 40 had a lump in the neck and six had contralateral hemiparesis.[2]

In our case reports: ***Case No. 1*** The aneurysms were most likely congenital because of their being multiple in number and the presentation as right sided hemiplegia and aphasia which improved with antiplatelet drugs and physiotherapy. Younger age also favours contgenital nature of aneurysms.

Case No. 2: Again the patient was a young female, multiparous with no history of intake of oral contraceptives. Other causes of "abnormal loop" being also ruled out. This is obvious that the "loop" was congenital and the hemiparesis that improved with antiplatelet drugs and physiotherapy was due to thromboembolism or slowing of circulation through the "ring shaped loop".

In every patient of cerebrovascular accident undergoing cerebral angiography (conventional or MRI), extracranial carotid artery should be visualized to exclude aneurysms or abnormal loop as a cause for stroke.

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Bullet Injury Causing Rupture of Spleen with Hydatid Cyst

N.A.Wani, MS; Saleem Tak, MS; N.D. Shah, MS; Adil Bashir, M.B.B.S; S.M.Arif, MS.

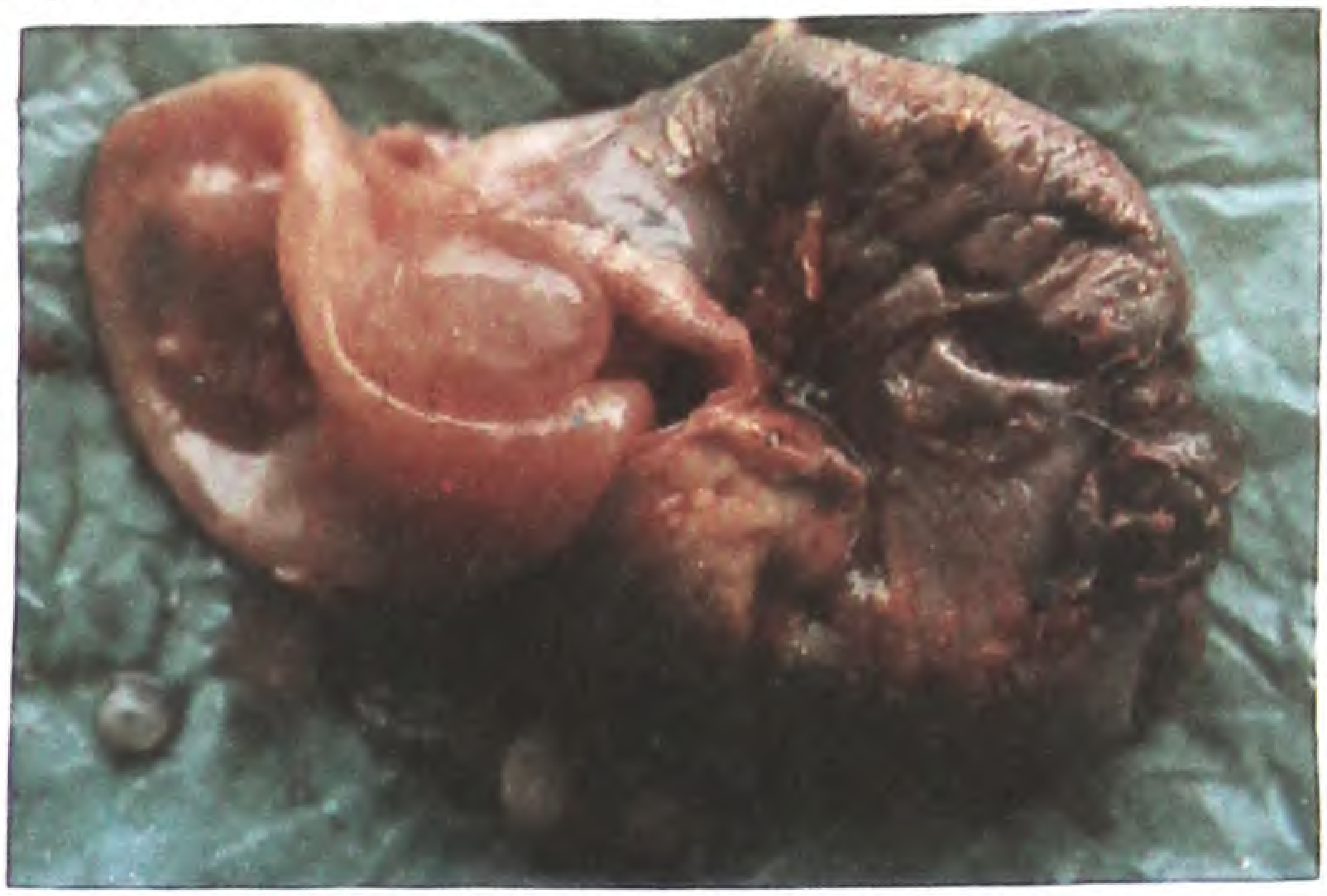
Abstract *: Hydatid cyst of spleen is uncommon in clinical practice, usual presentation being the mass in the abdomen. Fire arm injury causing the rupture of spleen containing a hydatid cyst is not reported. Here we report a case of this entity.*

Key Words: Hydatid cyst, Rupture spleen, Fire arm injury.

JK-Practitioner 1998; 5(1): 55-56

Case Report

A 55 years male presented to us with bullet injury left lower chest posteriorly within half an hour after injury. General physical examination revealed a grossly pale patient, in respiratory distress and shock. Examination of chest showed decreased air entry on left side and air sucking wound of exit on back of left lower chest. Examination of abdomen revealed guarding and tenderness in the left upper quardrent. Investigations revealed, fall in haematocrit and chest X-ray showed haemopneumothorax in left side. Thoracostomy tube was put in and abdominal paracentesis was performed which revealed haemoperitoneum. Emergency laprotomy was performed. After abdomen was opened numerous daughter cysts and blood were found in the peritoneal cavity. Spleen was found ruptured having multiple tears in its parenchyma. A big ruptured cyst was found along its superior medial region; laminated membrane projecting from the tear of adventitious layer. No other organ was seen injured.



Spleen showing multiple tears with ruptured hydatid cyst and prolapsing laminated membrane.

Another big hydatid 15cms/10cms in the liver was found intact. Rest all viscera were normal. Patient was given adrenaline and I/V corticosteriods and spleen along the cyst was removed. Peritoneal lavaging done. Post-operatively patient was put on albendazole for 4 weeks.

Discussion

Hydatid cyst is commonest in the liver with incidence more than 70 percent, followed by lungs, kidneys and bones. Hydatid cyst of spleen is uncommon in clinical, practice with incidence about 1 percent.[1] Hydatid cyst of liver is treated by either percutaneous drainage although still under clinical trials or operative enucleation of the cyst or partial liver resection.[2,8] For hydatid cyst of spleen recommended treatment is splenectomy. Rupture of hydatid cyst which may occur due to blunt trauma or iatrogenic trauma causes spillage of contents of the cyst into the peritoneal cavity which can give rise to severe anaphylaxis,

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peritonitis and dissemination of daughter hydatid cysts into the peritoneum.[4] Anaphylaxis is treated conventionally. Albendazole a benzimidazole, has been shown to be effective in human hydatid disease. The drug produces high concentrations of albendazole sulfoxide in the blood, cyst fluid and cyst wall which causes death of the scolices. Albendazole can be given for prevention of both recurrences and dissemination.[5]

In cases of blunt trauma particularly in children methods of conservation of spleen like splenorrhphy and partial splenectomy are used inorder to get rid of overwhelming-postsplenectomy infection (OPSI). The frequency of OPSI in adults is not known.[6] Penetrating trauma of spleen which includes firearm and sharp weapon injuries are mostly associated with injuries to other viscera although isolated splenic injuries are also seen with good frequency.[6,7] High velocity weapons like bullets from SLR, AK-47, Pistols, Blasts are common causatives of injuries at a distance from impact are associated i.e. bullet entering lower chest may be associated with a liver tear on right side and a splenic tear on left side. Paracentasis of abdomen is helpful in determining the presence of haemoperitoneum. Lapartomy is mandatory in cases of haemoperitoneum and presence of wound of exit or entry when on the abdomen.

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Unusual Presentation of Ascaris Lumbricoides

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Nazir Ahmad Malik, M.S.; Rekha Patnaik, M.S, MCh.

***Abstract** : Meckel's diverticulum is a relatively common congenital abnormality occurring in 1-3% of population [4,6]. Inflammation of the diverticulum closely simulates the clinical features of acute appendicitis. The actually inflammed diverticulum may proceed to perforation with localized abscess or generalized peritonitis. We report a rare case of peritonitis following perforation of Meckel's diverticulum by a round worm.*

Key Words: Meckel's Diverticulum; Peritonitis; Ascariasis lumbricoides.

JK-Practitioner 1998; 5(1): 57-58

Introduction

Meckel's diverticulum is an embryonic derivative of vitelline duct. It has been reported in various series to have an incidence of 1-3%. In most cases, Meckel's diverticulum is an incidental finding at post mortem or laprotomy. When symptoms occur, clinical manifestations vary with the type of complication present and in most cases diagnosis can be made with certainty only at operation. The symptomatic presentations are secondary to haemorrhage, small bowel obstruction, diverticulitis, associated umbilical abnormalities, tumours and perforation. Most of these complications are seen in paediatric age group. Foreign body may lodge in diverticulum and may lead to diverticulitis and perforation [1]. Even acute obstructive Meckel's diverticulitis can occur due to ascaris lumricoides [9,14].

Case Report

2 1/2 year old female was admitted in Paediatric Surgery Department of Sher-i-Kashmir Institute of Medical Sciences, Srinagar, Kashmir with the chief complaints of pain abdomen and vomiting (worms with vomitus) of 6 days duration, constipation, abdominal distention and fever of 3 days duration. Exact nature of pain could not be elicited because of age of patient. Patient was managed as worm obstruction at peripheral hospital and referred to SKIMS after he failed to respond to conservative line of management. Clinical examination of the patient revealed a high pulse rate, tachypnoea and high grade fever. Abdominal signs revealed features of acute peritonitis.

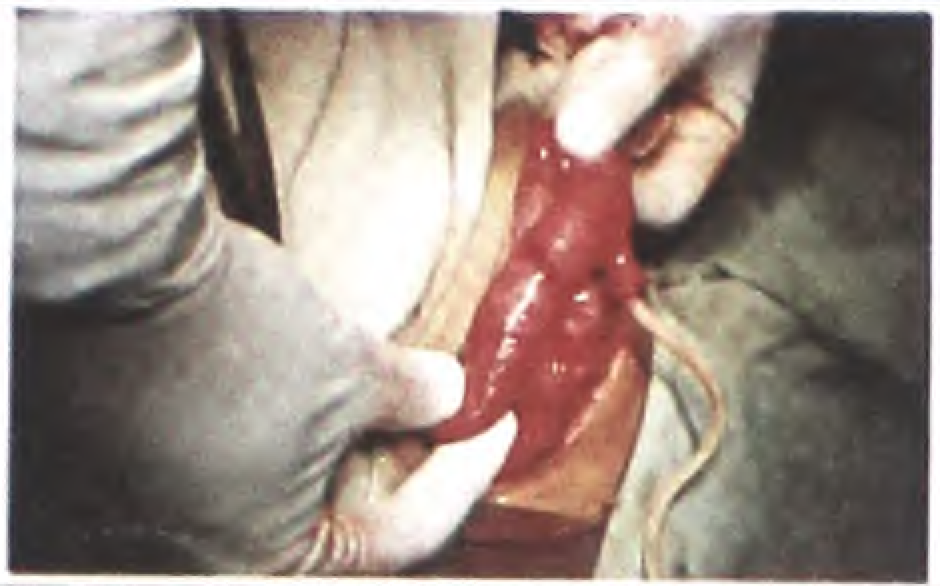

Fig. II : 2 Ascariasis seen, one in Meckel's Diverticulum and other one in general peritoneal cavit

Biochemical investigations revealed TLC of 11,000/cmm with 86% polys and normal serum chemistry. X-ray abdomen showed an isolated dilated loop of jejunum only with no gas under right dome of diaphragm. On exploration peritoneal cavity was full of purulent material (2 liters) with numerous round worms in general peritoneal cavity. Small bowel was matted together with pus flakes and interloop worms. Meckel's diverticulum was seen perforated with a worm coming out of it. Meckel's diverticulectomy with lavage of peritoneal cavity was performed. Post-operative period was uneventful.

Discussion

Meckel's diverticulum is a congenital diverticulum arising from failure of embryonic obliteration of vitelline duct connecting fetal gut to yolk sac that normally occurs during 5th to 7th week of gestation. It is estimated that only 4% of patients who possess Meckel's diverticulum become symptomatic during their life time [1]. Pathological complications of Meckel's diverticulum are related directly to the particular pattern of vitelline duct abnormalities. Thus they can mimic many intra-abdominal condition. Meckel's diverticulum should be considered as a possible cause of any intra-abdominal disease in which diagnosis is not evident

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[8]. The complications include, bleeding, obstruction, diverticulitis and tumours in addition to associated anamolies. The diagnosis is seldom made pre-operatively with certainty except in case of lower gastro-intestinal bleeding in paediatric population. Pattern of complication is also age related, with bleeding most common in children (75%) before 10 years of age and rare after age of 30 years. Small bowel obstruction may occur at any age. Diverticulitis accounts for 20% of case with peak incidence in older children. The incidence of complication is also related to the gender of the patient with complications rate observed 2-3 times more frequently in males. The actually inflamed diverticulum can proceed to perforation with localized abscess or general peritonitis. Peritonitis may also follow perforation of peptic ulcer of diverticulum or foreign body perforation.

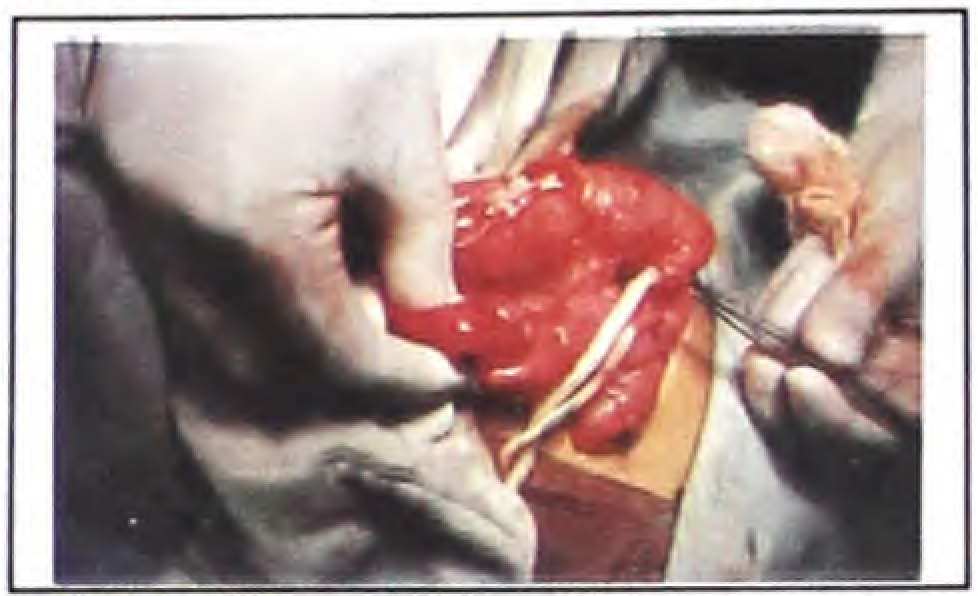

Fig. I : Ascaris lumbricoides seen coming out or performated Mackel's Diverticulum

W.G. Ninawe has reported acute obstructive Meckel's diverticulitis due to ascaris lumbricoides [14]. A case of Meckel's diverticulum with a worm in the general peritoneal cavity [10] has been reported. However, the site of perforation could not be located. M. R. Sareevastha has also seen a case of Meckel's diverticulitis caused by round worm incarcination. Roswick reviewed 50 case reports of foreign body perforation of Meckel's diverticulum, 28 of them were due to fish bones and other foreign bodies included cherry stone, a knitting needle, a gramophone needle, a wooden splinter and a chicken bone. Rutherford and Akers reported 3 cases of perforated Meckel's diverticulum (2 from peptic ulceration and 1 from a pin) [11].

Meckel's diverticulum can be identified pre-operative by radio-nuclear scanning [3] barium contrast studies, arteriography and occasionally computed tomography with varying degree of success.

The diagnosis of Meckel's diverticulum is occasionally suggested on plain abdominal film on the basis of an enterolith or radioopage foreign body in the right lower quadrant or sub-umbilical gas collection. Perforation of Meckel's diverticulum may result in gas under right dome of diaphragm.

Management of Meckel's diverticulum found incidentally on laparotomy in controversial [5]. There is a general agreement that diverticulum that appears to have heterotrophic mucosa on physical examination should be resected because of higher risk of subsequent complication [2,7]. Diverticulum with a narrow neck and with foreign body within it should also be resected. Finding at laparotomy indicating prior diverticulitis including scarring or adhesions should also dictate excision.

In summary careful review of medical history and increasedindex of suspicion coupled with diagnostic aids should help in arriving at diagnosis of Meckel's diverticulum and its complication.

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Christ Siemens Touraine Syndrome-A Case Report

Qazi Masood MD; Iffat Hassan MD.

***Abstract** : Two siblings with classical features of Christ Siemens Touraine syndrome are being described. Both of them seem to have inherited the disorder in an autosomal recessive pattern which is a very rare mode of transmission of this disorder.*

Key words : Ectodermal dysplasia, Autosomal recessive.

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Introduction

The ectodermal dysplasias is a group of disorders characterized by a primary defect in hair, nail, teeth or sweat gland function. About forty distinct syndromes have been encompassed under the heading of ectodermal dysplasias.[1] Out of them, Christ Siemens Touraine syndrome or anhidrotic ectodermal dysplasia is a form of ectodermal dysplasia characterized by partial or complete absence of sweat glands, hypotrichosis and hypodontia. The syndrome is usually inherited in an x-linked recessive form.[2] Rarely the disorder has been reported to occur in an autosomal recessive fashion.[3] Here, too we are reporting two siblings who seem to have inherited this syndrome in an autosomal recessive pattern.

Case I

An eight year old female, a product of a consanguinuous marriage presented with complaints of intolerance to heat and absence of hair over the extremities since early childhood. Morever, she had been having recurrent respiratory tract infections since infancy. Her milestones had developed normally. However, dentition was delayed and only eight permanent teeth had erupted. Deciduous teeth were conspicuous by their absence. The patient's scholastic performance was good. General physical examination revealed dysmorphic features like prominent chin and frontal ridges, saddle nose, slightly everted lips and large ears. Upper jaw comprised of only six teeth which included two each of incisors, canines and molars. The incisors and canines were widely spaced. (Fig. I) The lower jaw was conspicuous by total absence of teeth since birth. Cutaneous examination revealed absence of eyelashes and hair over the trunk and extremities. Eyebrows and scalp hair was sparse and light brown in colour. Fine wrinkling around the eyes and hyperlinearity of palms and soles was also noticed. Rest of the systemic examination was unremakrable. Skin biopsy from dorsal aspect of the forearm revealed absence of any adnexa.

Case II

A ten year old male, elder sibling of case I presented with a history of intolerance to heat since early childhood. Further probing revealed a history of recurrent respiratory tract infections since infancy. Dentition was delayed. His scholastic performance was very good. General physical examination revealed prominent frontal ridges, large ears and slightly everted lips. Cutaneous examination was conspicuous by absence of eye lashes, eye brows, hair over trunk and extremities. Dental examination revealed conical upper incisors and canines which were widely spaced. Upper jaw comprised of two each of incisors, canines and molars. Lower jaw had only two molars. Rest of the teeth had not erupted. Hyperlinearity of palms and soles was also present.

Skin biopsy from Forearm revealed absence of any adnexa. Family history was conspicuous by presence of aforementioned dysmorphic features in paternal grandmother of the patients who herself was a product

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of consanguinous marriage. Rest of the family members were unaffected.

Discussion

The earliest descriptions of ectodermal dysplasia were given by Danz, Wedderburn and Thurnan. In 1913, Christ named the disorder as congenital ectodermal defect. Clouston classified the disorder into anhidrotic and hidrotic forms. Freire Maia had suggested that to qualify as ectodermal dysplasia, the disorder must demonstrate a primary abnormality of the hair, teeth, nails and eccrine glands, in addition to the other ectodermal signs such as abnormality of the ears, lips, dermatoglyphics or central nervous system,[4,5]

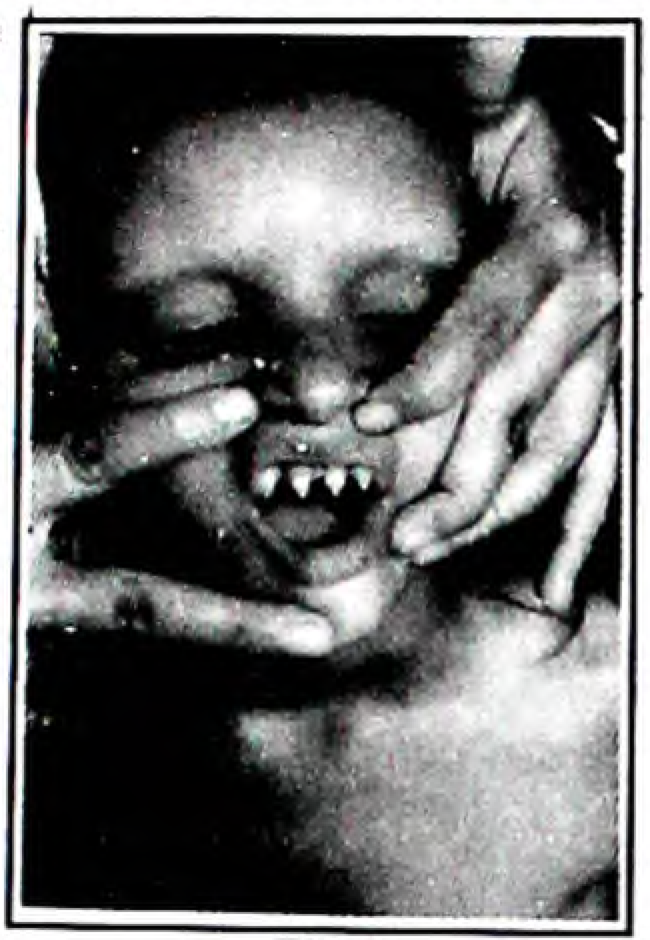

Fig I

The inheritance of anhidrotic ectodermal dysplasia or Christ Siemens Touraine syndrome is determined by an x-linked recessive gene.[2] It is characterized by absent or reduced sweating, hypotrichosis and total or partial anodontia. In the more complete forms the appearance of the patient is distinctive with prominent frontal ridges and chin, saddle nose, sunken cheeks, thick everted lips, large ears and sparse hair. The skin is smooth, soft, dry and finely wrinkled especially around the eyes. Heat intolerance is attributed to absent or reduced sweating and affected individuals may present with unexplained fever in infancy or childhood. Poor development of mucous glands in the respiratory and gastrointestinal tracts increases susceptibility to respiratory tract infections and may result in dysphagia, stomatitis and diarrhoea. Mental retardation has been reported to occur in 30-50% cases. The life expectancy is by and large normal.[6]

The siblings under discussion presented with complete form of Christ Siemens touraine syndrome and being products of a consanguinuous marriage they seem to have inherited the disorder in an autosomal recessive pattern which is an unncommon mode of inheritance of this disorder.

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Histoplasmosis - Its Treatment With Fluconazole

V.P. Venkatachalam, MS; Neena Chaudhary, MS.

Abstract : Histoplasmosis is the most common endemic mycosis in United States. It is rarely seen in India. Disseminated histoplamosis is usually seen in immunocompromised individuals such as those with HIV infection. We report a case of extensive rhino-oropharyngolaryngeal histoplasmosis with involvment of cervical lymph nodes in a HIV seronegative adult male. The treatement given along with a brief review of literature is discussed in the article.

Key Words : Histoplasmosis, Fluconazole, Endemic.

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Histoplasmosis is caused by a diamorphic saprophytic fungus, Histoplasma capsulatum. The disease is endemic in certain parts of United States. Till date, to the best of our knowledge, only seven cases of Histoplasmosis have been reported from India.[1]

Case Report

A 35 year old male patient came to Safdarjang Hospital with a two months old history of hoarseness. He also complained of oral ulcers and swelling on the right side of the neck.

Oropharyngeal examination revealed multiple ulcers over the buccal mucosa and the palate. There were multiple nodular lesions over the tongue. Indirect Laryngoscopy revealed multiple nodular lesions involving the valleculae, epiglottis, both the arytenoids and aryepiglottic folds, the false and the true vocal cords. Examination of the nose revealed a small nodular swelling in the right vestibule. There were three firm, mobile and non tender lymph nodes on the right side of neck. One of the submandibular lymph node was found suppurated. No abnormality was detected in general systemic examination. Liver and spleen were not palpable.

Routine haematological investigation revealed low haemoglobin 9.7 gm. percent. ESR was 52 mm FHR. Blood sugar was 90 mg%. Liver function tests and Kidney function test were normal. VDRL & Serological tests for HIV were negative. X-ray chest, X-ray PNS and X-ray soft tissue neck did not reveal any abnormality.

Biopsy was taken from multiple sites from oral and laryngeal lesions. Histopathological examination of the material showed a mass of non-caseating type of granuloma with areas of oedema and hyperaemia. There were multiple foci of histiocytes, fibroblasts and macrophages with giant cell formation. Staining with Periodic Acid Schiff stain revealed the presence of small round intracellular budding yeasts, whose morphology was consistent with that of Histoplasma capsulatum.

Patient was put on intravenous fluconazole 400 mg daily for 2 months. When all the lesions disappeared, the patient was switched over to oral fluconazole 400 mg daily which was continued for 6 months. Patient was closely monitored for any side effects through out the therapy.

Discussion

Histoplasmosis was first described in 1906 by Darling of Panama but he wrongly described the causative organism as a protozoon. Da Rocha Lima of Brazil identified and named the fungus as Histoplasma capsulatum in 1913.

The disease is endemic in certain parts of United States like Kansas, Missouri, Ohio, Indiana, Illinois and Kentucky. Seventy five percent of population in these areas may have a subclinical infection.[2]

Histoplasmosis has been reported to occur in old age and infancy[3,4] but Tiecke (1963) emphasised that there was no age predeliction for oral histoplasmosis.

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Young[4] (1972) observed that the oropharyngeal histoplasmosis occurs predominantly in males with a male to female ratio being. 6.5:1.

Disease manifestations range from asymptomatic infection to disseminated infection. It more commonly presents as a acute or chronic respiratory disease. Disseminated histoplasmosis is characterized by low grade fever, productive cough, splenomegaly, hepatomegaly and lymphadenopathy as the organism has predeliction for reticulo- endothelial system.

There is a general agreement among the otolaryngologists that oropharyngeal histoplasmosis occurs in chronic progressive type of disease.[4,6] Tiecke[5] further commented that oral lesions are usually accompanied by cervical lymphadenopathy. Laryngeal involvement also occurs in the chronic disseminated histoplasmosis. It may manifest as a submucosal mass, with or without ulceration and may result in hoarseness, dyspnoea or dysphagia.[7]

Disseminated histoplasmosis usually occurs in immunocompromised patients as those on steroid therapy, HIV seropositive patients, organ transplant recepients, diabetics and those with hodgkin's disease.[4,8]

Diagnosis of hisloplasmosis is based on clinical manifestations, skin tests for hypersensitivity to histoplasmin, laboratory tests for demonstration of antibodies to histoplasmin in serum. However, the mainstay in diagnosis is demonstration of the fungus in histopathological specimen and culture,[8] Histoplasma capsulatum stains well with Periodic Acio Schiff, giemsa or Gomori methenamine silver stain.

Traditionally, histoplasmosis has been treated with Amphotericin B in the dosage of 0.3 to 0.6 mg per Kg of body weight per day for 6-8 weeks. Amphotericin B is known to cause certain severe toxic effects like azotemia, hypokalemia,anaemia and acid base disturbance.[7,8]

The advent of newer imidazole derivatives such as Ketoconazole, Fluconazole and Itraconazole has revolutionised the management of histoplasmosis patients with fewer complications. Also, these drugs can be given orally, so that these patients can be treated on outdoor basis. Ketoconzole has been used for the treatement of disseminated histoplasmosis[9] and for laryngeal histoplasmosis.[10]

In our case, because of the involvement of multiple sites and the patient being HIV negative, we started the treatement with Intravenous Fluconazole 400 mg daily for 2 months after which the patient was switched over to oral fluconazole 400 mg daily for 6 months. All the lesions disappeared and no recurrence was observed till the last follow up.

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Anaesthetic Management of Eventration of Left Diaphragm

Akhtar Naqib MD; Suhaul Syeed MD.

***Abstract** : Eventration of the diaphragm (CDE) is a relatively rare disorder. It is a developmental abnormality that results in the muscular aplasia of the diaphragm. Estimates of the incidence are usually based on radiological surveys which cannot distinguish between the different etiologies of diaphragmatic elevation. Pulmonary hypoplasia similar to that associated with diaphragmatic hernia (CDH) also occurs in CDE, severe pulmonary hypoplasia and subsequent development of persistent pulmonary hypertension is a major contributing factor to mortality in these cases. We report a case of CDE which caused considerable respiratory distress after extubation necessitating active intervention post-operatively.*

Key words: Eventration of Diaphragm, Pulmonary hypertension, Respiratory distress.

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Case Report

A 20 months old male child weighing 10 kg was hospitalized with a history of repeated chest infection. The child had been noted to have cough with expectoration and recurrent bouts of loose motions during the 5 days prior to admission. On clinical examination, the child looked ill and weak. Routine biochemical and haematological investigations were within normal limits. Systemic examination revealed that apex was shifted to right side of sternum. On ausculation the heart sounds were heard on the right side (Dextrocardia) of the chest and air entry was diminished on the left side of chest. An abnormal air bubble resembling a gastric bubble was heard on the left lower mediastenium. Radiography of the chest revealed that trachea and mediastenium were shifted to right. Loops of intestine were seen on left side of chest (Fig.1). Heart shadow was not clear. Barium meal was done which showed barium in the intestines on left side of chest. A clinical diagnosis of eventration of left diaphragm was made and child was posted for surgery.

In the operating room the child was adequately sedated. A 20 G canula was inserted in one of the arm vein. A 22 G canula was inserted in the radial for monitoring an acid base gas (ABG). A pulse oximeter probe was placed and SPO_2 on room air was recorded. A modi field ECG lead system was monitored. The preinduction heart rate was 110/mt. The child was preoxygenated for 5 minutes and induced with thiopentone. Vacuronium was used for muscle paralysis, the child was intubated with 4mm endotracheal tube and anaesthesia was maintained with oxygen N_2o 50:50. The surgeon opened the abdomen through subcostal incision. The stomach spleen, colon and most of the small bowel were found to be within the left thoracic cavity. Which were returned to the abdomen and defect in the left hemidiaphragm was repaired. Vacuronium was reversed with Inj. Neostignine and Inj. Atropine. After a brief suction of the oral cavity the child was extubated without undue delay as the child was straining on the endotracheal tube and was wide-awake. Only 5 minutes after the extubation the child started becoming cyanosed. 100% oxygen was given via mask. The child's colour improved and was shifted to recovery room. The child again started getting respiratory distress. The child was intubated and manually ventilated again. Anterial blood gas analysis was sent immediately which showed slight acidosis which was corrected by Inj. Sodium Bicarbonate. The child was put on overnight ventilation in surgical ICU and was extubated next morning. His recovery was uneventful.

Discussion

Eventration of the diaphragm has been described as an abnormality high or elevated position of cone

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leaf of the diaphragm as a result of paralysis, aplasia or atrophy of varying degrees of the muscle fibre. It is classified etiologically into acquired (*paralytic* and congenital (*non paralytic*) forms. An acquired eventration is usually the result of a lesion of the phrenic nerve caused by birth trauma, operative injury, infection, inflammation or a neoplasm.

Pulmonary hypoplsia similar to that associated with diaphragmatic Hernia (CDH) also occurs in congenital diaphragmatic eventration. Severe pulmonary hypoplasia is a major contributing factor to mortality in these cases. Lung hypoplasia accompanying congenital diaphramatic defects is characterised by diseased number of air way and vascular ramifications and by delayed development of the alveoli. Gradual expansion of the hypoplastic lung and consequent alveolar over distension may result in the early closure and constriction of the small airways.

Administration of anaesthesia for patients with diaphragmatic eventration and diaphragmatic Hernia is always hazardous and challenging. Eventration of diaphragm is mostly repaired via a thoracotomy. Thoracotomy causes rigidity of the chest wall which may result in ventilatory restriction whereas residual or reccurent paradoxical movement of the diaphragm may limit ventilation in eventration. No attempt should be made to further expand the lungs when the eventration is reduced because this may cause increased and unnecessary pulmonary damage.

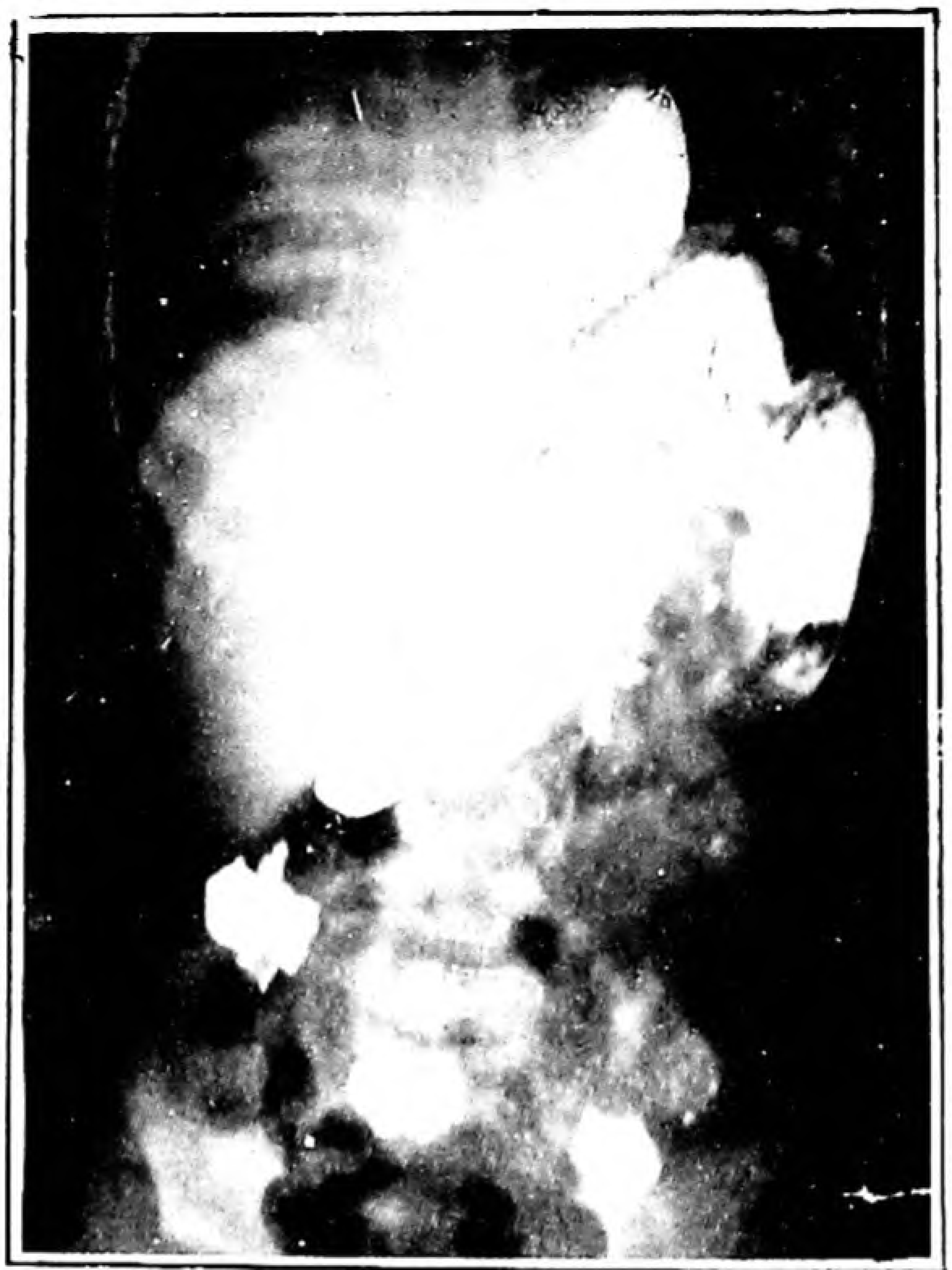

Fig. I - Chest X-ray with eventration of diaphragm showing gas filled abd. viscera in Lt. thorax.

The major determinants of outcome in these patients are the extent of pulmonary hypoplasia and the degree of pulmonary artery hypertension. In the post operative period some children will exhibit a 'Honey Moon' period which is then followed by a sudden unexplained clinical deterioration, with acidosis, Hypoxemia, hypercapnia, pulmonary hypertension, right to left shunting and death.

Therapeutic measures at this stage are aimed at decreasing pulmonary vascular resistance preventing left to right shunting. Such measures include hypoventilation, ligation of PDA and pharmacological therapy.

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Bi-Directional Differentiation of Colonic Tumours

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***Abstract** : A colonic tumour is presented with composite differentiation in which adeno-carcinomatous areas were associated with foci suggestive of Carcinoidal differentiation . It is suggested that this divergent differentiation is because the two elements differentiated from a common precursor.*

Key words: Adeno-carcinoma, Carcinoid, Argyrophilic, Argentaphilic.

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Case Report

A 25 years young male presented with complaints of anorexia, weight loss and bleeding per rectum. He was admitted to hospital and investigation revealed a growth hepatic flexure. On laparatomy a large polypoidal growth with ulcerated surface (4.5x 3.5 cm polypoidal ulcerated growth) involving the whole circumference of colon was seen.

On histological examination the tumour showed the morphology of a well differentiated adeno-carcinoma. However at one edge solid cell nests and cords composed of small uniform cells with modest amount of cytoplasm merged imperceptibly with adeno-carcinomatous portion. The adeno-carcinomatous acini and areas exhibiting carcinoid differentiation demonstrated a closed admixture. In addition to routine Haematoxylin-Eosin stains, Mucicarmine staining and Masson's Fontanna staining were used.

Discussion

The occurence of acinar structures within carcinoid tumours is well recognized. However, such acini differ from the carcinomatous acini which are lined by an epithelium which although columnar, is variable in size and stratification. Large and often irregular lumina are enclosed. The purely carcinoidal acini, by contrast are usually small and spherical or oval in shape. They are surrounded by the component carcinoid cells, or by a uniform, low cuboidal epithelium. In the present case, characterization of solid cords and nests as possible foci of carcinoid differentiation was dependent entirely upon their morphology as seen in haematoxylin- eosin preperations. The negative Masson's Fontanna staining in the present case cannot be regarded as exclusive of bi-directional differentiation of colonic tumours. The experience of others has indicated that many carcinoid tumours do, in fact, fail to yield postive results on specific staining. The morphological aspects of these possible areas of carcinoid differentiation exhibited a marked homogenicity which contrasted noticeably with the carcinomatous areas exhibiting a degree of pleomorphism. The occurence of glandular lumina within carcinoid tumours is well recognized.[1] However presence of argentaffin and argyrophil cells within gastrointestinal tract has previously drawn attention towards the composite nature of these tumours.[1-4]

The occurence of composite carcinoma-carcinoid tumour in the colon can be readily explained by the tumour arising from the multipotent stem cells showing bidirectional differentiation.[5]

It is suggested that intermingling of the two constituents depicts a close histogenetic relationship. It may be noted that the presence of argentaffin and argyrophilic cells within gastric carcinomata has previously been regarded as evidence of divergent differentiation within these tumours.[4]

It is also suggested that the possibility of dual composition discussed may have a wide applicability in relation to neoplasms of organs containing both endocrine and non-endocrine elements.[6] One has to be also aware of the possibility of endocrine trabecular component being on occasion mis-interpreted as

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anaplastic transformation within the adeno-carcinoma.

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CURRENT CLINICAL GUIDELINES

Peptic Ulcer Disease: Defining the Treatment Strategies in the Era of Helicobacter pylori

Richard H. Hunt, F.R.C.P., F.R.C.P.Ed., F.R.C.P.C., F.A.C.G.

Peptic ulcer disease continues to be a major health care problem costing the public billions of dollars each year. Recent evidence confirms a major role for Helicobacter pylori infection in the natural history of most cases of peptic ulcer disease. The most established and effective antibiotic treatment for the eradication of H. pylori has been the classic bismuth "triple therapy" regimen containing bismuth, metronidazole, and tetracycline. However, pretreatment resistance to metronidazole, poor compliance, and side effects have limited the wide-spread acceptance of bismuth triple therapy for routine use. Recent studies suggest that the combination of one or two antibiotic agents and a proton pump inhibitor offers a better tolerated regimen than bismuth triple therapy. Efficacy is similar with respect to eradication of H. pylori, and the combined use of a proton pump inhibitor assures rapid symptom relief and ulcer healing. Although the mechanisms by which. H. pylori eradication is effected, the optimal dosing schedules, and the specific antimicrobial agents to be administered require further study, the combination of a proton pump inhibitor and one or two antibiotic promises to be an appropriate first-line treatment for peptic ulcer disease.

Introduction

Despite dramatic advances in diagnosis and management over the past 20 years, peptic ulcer disease remains a major and serious health care problem, with approximately 500,000 new cases and 4 million recurrences each year in the United States.[1] Estimated annual direct costs related to the disgnosis and treatment of peptic ulcer disease are $3 to $4 billion,[1] compared with $2.5 million in 1975.[2] Indirect costs related to lost productivity are generally comparable to the direct costs.[3]

Helicobacter pylori has been identified in 90-95% of patients with duodenal ulcer and 60-80% of patients with gastric ulcer, compared with a 25-30% incidence in asymptomatic control subjects.[4-7] The prevalence of infection increases with age and is more common in those with deprived socioeconomic circumstances.[8] The lifetime prevalence for duodenal ulcer is approximately 10% for men and 5% for women.[9]

The pathogenesis of peptic ulcer disease is complex but essentially involves and imbalance between aggressive factors, especially gastric acidity, and defensive factors of the gastroduodenal mucosa.[10] A critical association between H. pylori infection and gastric metaplasia in the duodenal cap confers a predisposition to ulcer disease,[10-13] and strong evidence has accumulated showing an association between the cure of H. pylori infection and the cure of peptic ulcer disease.[10-15]

Although the exact role of H. pylori infection in the natural history of peptic ulcer disease remains to be defined more clearly, evidence indicates that colonization of the gastric antral mucosa by H. pylori results in an uninihibited secretion of gastrin as a result inhibitis gastrin synthesis and relsease, and lack of the somatostain brake on gastric secretion results in increased gastrin-mediated acid secretion.[10,11,13,16,17]. Mechanisms that have been proposed to explain the effect of H. pylori in lowering stainable somatostatin cells and somatostatin release include the following: 1) alkalinization of the gastric antral mucosa caused by the ammonia produced by the urease activity of H. pylori[16] or damaged epithelium leaking bicarbonate,[11] although an increase in intragastric pH alone provides little stimulation to the release of gastrin[13]; 2) release of bacterially derived amines from the metabolism of

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H. polyri and other bacteria[14]; and 3) increased expresion of major histocompatibility complex class II antigens on gastric epthelil cells, resulting in the release of inflammatory cytokines such as interleukin 1 (IL-1), 6, and -8, leukotrienes, tumor necrosis factor-a, and platelet-activatin factor.[11] Regardless of the mechanism involved, infection with H. pylori is associated with an increase in the postprandial release of gastrin and an increase in the overall area under the curve for gastrin throughout the whole 24-h period. It remains to be determined, whether, over time, the increase in gastrin results in an increased parietal cell mass and increased secretory capacity in duodenal ulcer patients. It is known that the presence of gastric metaplasia in the duodenum is associated with increased fasting intragastric acidity ($pH<2.5$) and when fasting pH is < 2.0, the areas of gastric metaplasia are increased. With exposure are increased concentrations of acid/pepsin, an epithelium damaged by H. pylori infection is vulnerable to ulceration.[10,11]

Therapeutic strategies for peptic ulcer disease hsitorically have focused on decreasing intragastric acidity with antisecretory agents such as the H2-receptor antagonists or, more recently, proton pump inhibitors.[18] With the increasing acceptance of the causative role of H. pylori infection in peptic ulcer disease, current therapy comprises antibiotic regimens in combination with antisecretory drugs to eradicate H. pylori and achieve enhanced healing of duodenal and gastric ulcer and dramatically reduced recurence.[10,12,14,15]

This review describes current antimicrobial regimens and antisecretory/antibiotic combinations for the treatment of peptic ulcer disease.

Table 1

Antibiotic Therapy Combinations for the Eradication of Helicobacter pylori in Patients with Duodenal Ulcer, Nonspecified, or Mixed Peptic Ulcer Disease, Gastritis, or Nonulcer Dyspepsia (19-21)

Therapy agent(s)	No. Studies	Therapy Duration (wk)	Eradication Rate (%)
Single			
Bismuth*	10	4-8	20
Amoxicillin	3	2-4	23
Clarithromycin	2	2	15-54
Double			
Bismuth* + Amoxicillin	7	2-6/1-4	44
Bismuth* + Metronidazole	4	1-4/1-2	55
Amoxicillin + Metronidazole	1	1/1	56
Triple			
Bismuth* + Metronidazole + Amoxicillin	6	2-4/1-2/1-2	73
Bismuth* + Metronidazole + Tetracycline	3	3-4/1-2/2-4	94
Furazolidone + Metronidazole + Amoxicillin	1	5/5/5 days	54

* Colloidal bismuth subcitrate or bismuth subsalicylate.

! Eradication rates varied with dosage regimens; 15% with 500 mg *b.i.d.*, 42% with 250 mg *q.i.d.*, 36% with 1000 mg *b.i.d.*, and 54% with 500 mg *q.i.d.*

Bismuth-Based antimicrobial therapy

In vitro, H. pylori is sensitive to a wide variety of antimicrobial agents, including macrolides, B-lactams, tetracycline, metronidazole, tinidazole, rifampicin, gentamicin, nitrofuran, and some quinolones.[10,13] However, attempts to eradicate H. pylori with any one of these agents administered as monotherapy have generally proved very disappointing (Table I)[10,13,19]. Eradication rates are of the order of 20%, although rates up to 54% have been reported for clarithromycin, a new macrolide antibiotic that is well tolerated and more acid stable than erythromycin[19-21]. Improvement in the rates of cure of H. pylori infection may be achieved with the addition of one or two antibiotics to the therapeutic regimen, with the more commonly administered combinations being the classic bismuth triple therapy of bismuth subsalicylate or subcitrate, and metronidazole in combination with tetracycline or amoxicillin (standard bismuth triple therapy) (Tabe I)[13,19,22]. Administration of classic bismuth triple therapy has had some limitations. Amoxicillin has proved to be significantly less effective than tetracycline in eradicating H. pylori infection.[19] Meta-analysis of these two combinatiuons has shown that triple therapy incorporating tetracycline achieves a significantly higher H. pylori eradication rate (94.1%) than that incorporating amoxicillin (73.1%).[19] Pretreatment resistance to metronidazole is also a problem, especially in parts of Europe and Africa, where community resistance has a high prevalence.[23] Compliance is an important factor influencing the success of bismuth triple therapy.[22] In one study, involving patients with duodenal ulcer, gastric ulcer, or gastritis, a 96% eradication rate was observed for patients who took at least 60% of their prescribed medication compared with 69%.[22] Compliance with bismuth triple therapy may be hindered by the frequent dosing required and by dosing that may involve up to 18 tablets a day, with adverse events reported in an average of 32% of patients in clinical trials.[13,19,24]

Antibiotic and Acid-Suppressive Combination Therapy

Treatment regimens for H. pylori infection that are as effective as bismuth triuple therapy but simpler to administer, easier to tolerate, and that are associated with better compliance could combine any of several antibiotics with an antisecretory drug (Table 2).[13,25-30]

Table 2
Antibiotic/Acid-Suppressive Therapy Combinations for the Eradication of Helicobacter pylori (25-30, 37)

Reference	Agents	Eradication Rate, % (No.)
Graham *et al.* (25)	Ranitidine + Bismuth + metronidazole + Tetracycline	85 (40/47)
Burette *et al.* (26)	Lansoprazole 30 mg (4 wk) + roxithromycin 300 mg/ metronidazole 500 *b.i.d.* (14 days)	82 (14/17)
Cayla *et al.* (27)	Lansoprazole 30 mg. *b.i.d.*/ amoxicillin 1 g *b.i.d.*/ clarithromycin 500 mg. *b.i.d.* (14 days)	95 (20/21)
	Lansoprazole 30 mg *b.i.d.*/ amoxicillin 1000 *b.i.d.* (14 days)	33 (8/24)
Bayerdorffer *et al.* (28)	Omepraxole + amoxicillin	82 (22/27)
Logan *et al.* (29)	Omeprazole + Clarithromycin	78 (57/73)
Takimoto *et al.* (30)	Lansoprazole 30 mg + clarithromycin 200 mg. *b.i.d.* (14 days); lansoprazole 30 mg (4-6 wk)	50 (11/22)
	Lansoprazole 30 mg *b.i.d.* + clarithromycin 200 mg; lansoprazole 30 mg (4-6 wk)	74 (14-19)
Hentschel *et al.* (37)	Ranitidine 300 mg (6 or 10 wk) + amoxicillin 750 mg/ metronidazole 500 mg. *t.i.d.* (12 days)	89 (46/52)

The antimicrobials with more effectiveness in a combination regimen include amoxicillin, tetracycline, clarithromycin, and metronidazole.[12,19,22]

In the pathogenesis of peptic ulcer disease, gastric acidity is still considered to play a major etiologic role in ulceration, and antisecretory drugs continue to be the mainstay of therapy. Proton pump inhibitors have greater efficacy than other classes of acid-suppressing drugs in the management of peptic ulcer disease and achieve rapid symptom relief and ulcer healing.[31,32] The results of some recent studies suggest that antibiotic/ antisecretory drug combinations that include a proton pump inhibitor, as opposed to an H2-receptor antagonist, provide better eradication of H. pylori infection (Table 2). For example, the combination of a proton pump inhibitor and one or two antibiotic agents can achieve H. pylori eradication rates comparable to those obtained with bismuth triple therapy.[13,26,31] Furthermore, these regimens were associated with less antimicrobial resistance, higher patient compliance, and fewer side effects than are usually observed in trials with bismuth triple therapy.[13,19,22-24,26,29,33]

Lind *et al*. have shown that a proton pump inhibitor combined with clarithromycin and a nitromidazole administered for 1 wk achieved H. pylori eradication rates in excess of 90%.[34] Their MACHI study demonstrated that a treatment regimen comprising omperazole, metronidazole, and clarithromycin, or omeprazole, amoxicillin, and clarithromycin achieved eradication rates of 95 and 96%, respectively, in comparison with a 79% eradication rate with omperazole, amoxicillin, and metronidazole.[34] Further studies, particularly in the United States, are needed to confirm these early results.

Although concomitant administration of a proton pump inhibitor and one or two antibiotic agents enhances antibiotic activity, pretreatment with omprazole seems to decrease H. pylori sensitivity to amoxicillin.[13,33,35,36] For example, Labenz et al. reported an eradication rate of 29% when amoxicillin was administered during the second 2 wk of a 4-wk course of omeprazole treatment compared with 83% when the same dose regimens were administered in combination simultaneously for the initial 2-wk period.[33] The investigators suggested that pretreatment with omeprazole may induce persistent coccoid forms of H. pylori.[33] There is, to date, no such data to suggest that this effect occurs with antibiotic other than amoxicillin.

Graham and co-workers reported that the

combination of the H2-receptor antagonist ranitidine and bismuth triple therapy improved duodenal ulcer healing with compared with the administration of ranitidine alone. H.pylori eradication rates were comparable to those previously reported for classic bismuth triple therapy (Table 2).[19,22,25] In a study by Hentschel et al., in which patients received ranitidine nightly for 6 or 10 wk in combination with metronidazole and amoxicillin for the first 12 wk, respectively.[37] Patients receiving ranitidine and polacebo showed healing rates of 75 and 94%, respectively. H. Pylori eradication rates were 88 and 2%, respectively, and ulcer recurence was reduced to 8 and 86%, respectively. For those patients who were confirmed as being H. pylori negative after treatment, the ulcer recurrence rate was only 2%. Despite the encouraging results of this small study, other studies with an H2-receptor antagonist and similar antimicrobial regimen have shown an average eradication rate of 74%.[38]

Proton Pump Inhibitors and H. Pylori

H. pylori eradication rates produced by the combination of a proton pump inhibitor and one or two antibiotic agents are higher than those observed in some regimens containing one, two, or three antibiotics with or without other classes of antisecretory drug (Table 1 and 2)[19-21,26-30] Proton pump inhibitors may augment the action of antimicrobial agents through several possible mechanisms, including a direct effect on the organism and also by changing the gastric environment.

All the proton pump inhibitors, including omeprazole, lansoprazole, pantoprazole, and E3810, unlike the H2-receptor antagonists, have in vitro activity against H. pylori.[12,39] The minimum inhibitory concentration (MIC_{50}) against H.pylori was determined to be 3.1 ug/ml to 12.5 ug/ml for lansoprazole, which is comparable to that of bismuth subcitrate and more potent than omprazole (25-50 mg/ml).[13,31,39] In vitro, both lansoprazole and omeprazole selectively inhibit H. pylori urease, which is essential for gastric colonization by H. pylori.[40] However, it is not yet clear how the in vitro activity of proton pump inhibitors applies to the in vivo situation,[13] because the in vitro activity of antimicrobials against H. pylori in general does not predict in vivo efficacy.

More recently, it has been shown that the proton pump inhibitors are also active against a "p"-type ATPase identified in H. pylori.[14] It remains to be determined whether this is an important additional mode of action of the proton pump inhibitor acting in synergy with antimicrobials in vivo.

The pH elevation afforded by proton pump inhibitors may reduce the degradation of both acid-labile antibiotics and H. pylori-specific immunoglobulins,[42] while also decreasing the pH gradient across the mucus bicarbonate layer and enhancing the environment at the epithelial cell surface for neutrophil function.[13,43] Furthermore, the reduction of gastic acid juice volume produce by high-dose proton pump inhibitors will enhance the concentration of antibiotics in the stomach.

Conclusions

The mechanisms of action of antimcrobial regimens including protom pump inhibitors for H. pylori eradication still need to be elucidated fully, and optimal dosing regimens for the various combinations of antibiotic/proton pump inhibitor need to be determined through further clinical studies. However, the combination of a proton pump inhibitor and either amoxicillin or clarithromycin is appropriate as first line management of peptic ulcer disease in the primary care setting. Such a therapeutic regimen provides H. pylori eradication rates varying from 55 to 80%, with fever side effects than bismuth triple therapy. Moreover, this approach achieves rapid symptom relief and reliable ulcer healing. The combination comprising a proton pump inhibitor, clarithromycin, and a nitromidazole may achieve an eradication rate of about 90% but additional studies in the United States are needed to confirm these exciting early results.

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HIV Update

In 14th century, bubonic plague killed 25 million persons. Early 29th century Inflenza killed 20 million people. It now seems that HIV has infected 28 million people and by the end of this century will become the greatest lethal epidemic in the history of civilized world.

Mechanism for Transmission of HIV in 1997

☞ Sex inter course	70%
☞ Infection drug abuse	27%
☞ Blood transfusion	2%
☞ Haemophilia	1%
☞ Perinatal transmission	1%
☞ Occupational transmission	
☞ House hold contacts	
☞ Artificial insemination	
☞ Transmission from health care workers to patient	
☞ No mechanism defined	

Guidelines for HIV Therapy in 1997

1. When to start therapy:
   (a)In acutely infected patients at the time of acute HIV infection or within 6 months of sereconversion.
   (b)In chronically infected when HIV RNA levels$\geq$10,000 copies/ml.
2. What therapy to start:
   Preferred: 2NRTIS (AZT plus 3TC, AZT plus dd1, AZT plus ddc, 3TC plus d4T, or dd1 plus 1 protease inhibitor (retinovir, indinavir, nelfinavir)
   Alternative:(Somewhat effective): 2 NRTIS plus nevirapine.

Second alternative (considered standard but preferable to no therapy in some patients) 2NRTIS:

Contraindicated : Monotherapy with any agent, combination of AZT plus d4T, dd1 plus ddc, or ddc plus d4T.

Treatment failure . (HIV RNA level) 500 Copies/ml. 4 to 6 months after initiating treatment. Toxicity or non-acceptance of treatment.

Therapy for treatment failure:

Previous therapy	New therapy (new drugs)
2 NRTIS plus protease inhibitor	2 new NRTIS plus new protease inhibitor. 2 new NRITS plus nevira pine New protease inhibitor plus nevirapine plus new NRTIS 2 new protease inhibitor with or without NRTIS
2 NRTIs nevrirapine 2 NRTIs	2 new NRTIS plus prostease inhibitor 2 new NRTIS plus prostease inhibitor or nevirapine

3TC = Lamivudine; AZT = Zidovudine;
4dt = Stavudine: ddc = Zalcitabine;
ddl = Didanosine: NRTI = Nucleoside reverse transcriptase inhibitor

10 Most improtant developments in HIV-related diseases

1. Introduction, use and impact of protease inhibitors.
2. HIV RNA levels relevance to prognosis.
3. New drugs and immune modulatin.
4. Concept of cure as a possibility.
5. 100% condom compaing - reduction of transmission in Thailand.
6. Reduction of vertical transmission.
7. New strategies for prophylaxis against Mycobecterium avium complex with clarithromycin and azithromycin.
8. Herpesvirus 8 cultivation and implication in Kaposi sarcoma.
9. Demonstration that provides experience increase patient survival.
10. Reduction in transmission with occupational exposure plus new guidelines.

Source : Ann Int. Med 1997; 127:(Aug) 271-224. Infection update.

IMAGING TODAY

Stereotactic Large - Core Breast Biopsy

Arfa Khan, M.D.; Peter Herman, M.D.; Frances Vernace, M.D.

With more women participating in screening programs, there is an ever increasing number of abnormalities detected on mammograms. Despite advances in mammographic technique, it remains difficult to correctly predict the benign or malignant nature of mammographically detected breast lesions and therefore a biopsy is frequently required. Surgical excisional biopsy is currently the most common type of breat biopsy and is considered the gold standard for breast disease diagnosis. Approximately one million women per year undergo surgical breast biopsy nationwide. Only ten to fifteen percent of mammographically detected suspicious breast lesions prove to be malignant by open surgical biopsy. Consequently, nine often women undergo surgical biopsy for benign disease.

Surgical biopsies can be performed on an in-patient basis and under either general or local anesthesia. Surgical biopsy for non-palpable, mammographically detected abnormalities requires a pre-operative needle localization under mammographic or ultrasound guidance. The surgeon uses the needle or wire as a guide to locate the lesion in the breast, which is then removed with the surrounding tissue. Under ideal circumstances, an average diameter of 6 cm of tissue is removed, however, in many cases more than 25 cm is removed. Under local anesthesia, this can still result in as high as a 20% lesion miss rate.

Fine needle aspiration biopsy (FNAB) of breast lesions has been advocated to reduce the number of unnecessary surgical procedures. Patients whose FNAB reveals no evidence of malignancy might be followed

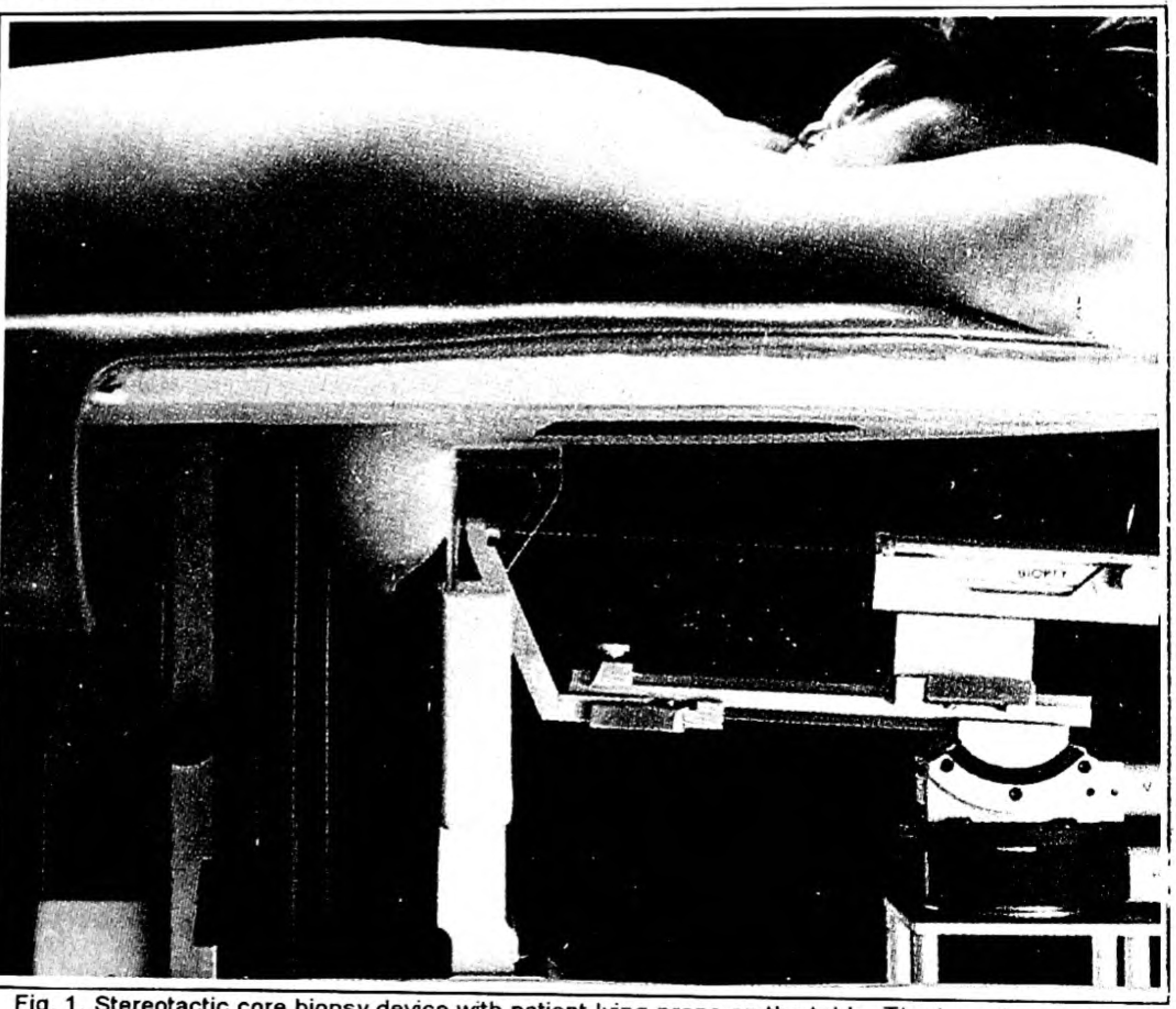

Fig. 1. Stereotactic core biopsy device with patient lying prone on the table. The breast protudes through an opening in the table. The biopsy device is located under the table, out of sight of patient.

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From the Long Island Medical Centre, New Hyde Park, New York.
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closely rather than subjected to surgical excisional biopsy. Aspiration breast biopsy is usually performed with a 21-23 gauge needle to which a syringe can be attached. After the needle is placed in the area of interest, a vacuum is created and multiple up and down needle motions are performed. Three or more passes are usually made. Smears are then made on glass slides and the specimen fixed and stained. A highly skilled and tained cytopathologist is needed for interpretation. There are, however, drawbacks of FNAB of the breast. These include insufficient tissue for diagnosis in a substantial number of cases (6-47%), significant percentage of false positive results (1-31%), occasional false positive results (1%), the limited ability to make a definite benign diagnosis and the difficulty in precise classification of the malinancy present. For these reasons many patients require surgical excisional biopsy as well, thus adding to the cost of breast cancer diagnosis.

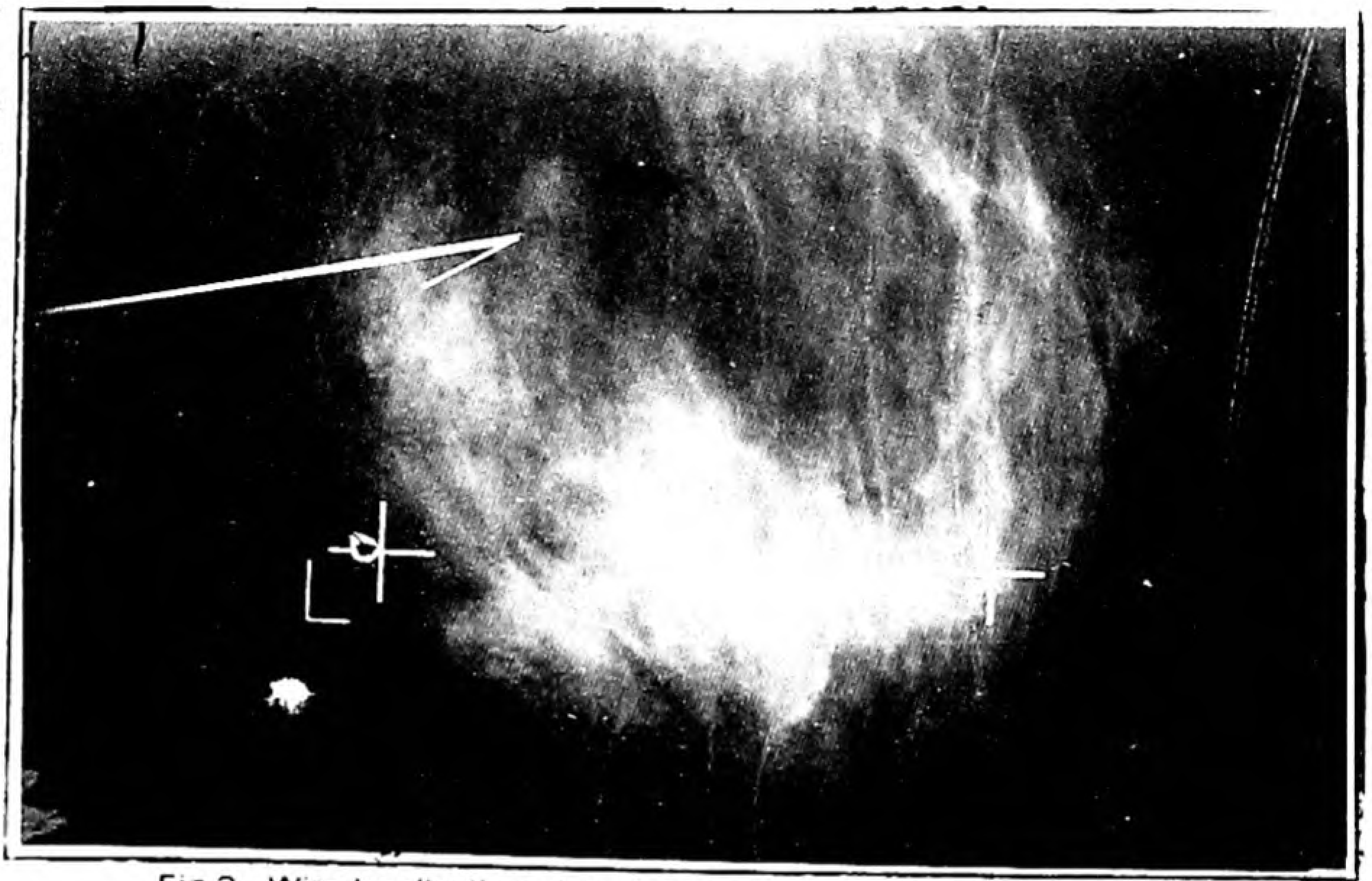

Fig 2. Wire localisation of the lesion (arrow) prior to surgical biopsy.

Stereotactic large-corebiopsy of non-palpable breast lesions overcomes many of the drawbacks of FNAB. The use of a 14 guage biopsy needle allows a sufficient volume of tissue for a definitive pathologic diagnosis. There are no false positive diagnosis. Since core tissue allows for histologic analysis, definitive benign diagnoses can be made. Additionally, exact classification of a malignancy can be accomplished with histological evaluation of core tissue which allows for better surgical management of the patient. The technique of stereotactic core biopsy was first developed in Sweden and is now increasingly used for diagnosis of non-palpable breast abnormalties in the USA. Recent studies comparing stereotactic core biopsy with excisional surgical biopsy of breast have shown that the accuracy of core biopsy is comparable to surgical biopsy. Stereotactic core biopsy however, has definite advantages over open surgical biopsy. The procedure takes less time to perform. There is no incision or scar, no anesthesia is required, the potential for complications is minimal and the cost is 25-50% less than surgical biopsy. However, not all patients are suitable for stereotactic core biopsy. Patients with very small breast (compression< 2cm) or with diffused calcifications are not suitable candidates for core biopsy. Deep lesions, close to the chest wall may not be accessible for biopsy with this technique.

Technique

Stereotactic large core biopsy ideally requires a dedicated stereotactic device (Fig. 1). The patients lies face down on a padded table with the breast protruding through an opening in the table. The compression plate, X-ray tube, and the stereotactic biopsy apparatus are located under the table, out of sight of the patient. The first step in the stereotactic core biopsy sequence is to obtain a mammographic localizing view to ensure that the lesion is located within the aperture of the compression plate. Stereo views are then obtained by swinging the x-ray tube 15 degrees off center in each direction. The two stereo images are exposed adjacent to each other on the same film. The stereo views are used to calculate the coordinates on a digitizer. A hand held computer mouse is activated at the center of the lesion and at reference coordinates in each stereo view. The digitizer prints out the horizontal, vertical and depth coordinates.

The biopsy gun is then locked into the dedicated housing and the coordinates are dialed into the main unit. The gun and needle align automatically on the proper trajectory. The skin over the puncture site is anesthetized with 1% lidocaine and a small skin nick is made through which a 14 guage biopsy needle can pass. The needle is advanced to the calculated depth and stereoviews are obtained to confirm the position of the needle in relation to the lesion. The gun is then fired by pushing the button and the biopsy is performed with split second sampling. A final set of stereo views are obtained to confirm that the needle has traversed the lesion. The needle is removed and the core tissue obtained is placed in sterile saline. Five or more passes are made in measured increments from the center of the lesion depending on the nature and size of the lesion. All biopsy passes traverse the same skin nick. The biopsy gun has a two phase action. At a very high speed the inner trocar, with the 16 mm long sampling chamber, is thrust forward a distance of 23 mm. This is followed almost immediately by a similar 23 mm forward thrust of the outer needle, cutting off the tissue core. The rapid fire nature of the device allows penetration of a very firm and/or fibrotic lesion before it can slip out of the needle path. The biopsy cores are well defined and measure approximately 1.5 cm to 2.5 cm in length and 2 mm in diameter. The procedure is painless and well tolerated. The woman can resume her normal daily activity following the procedure. There are no major complications and no premedication or sedatives are needed.

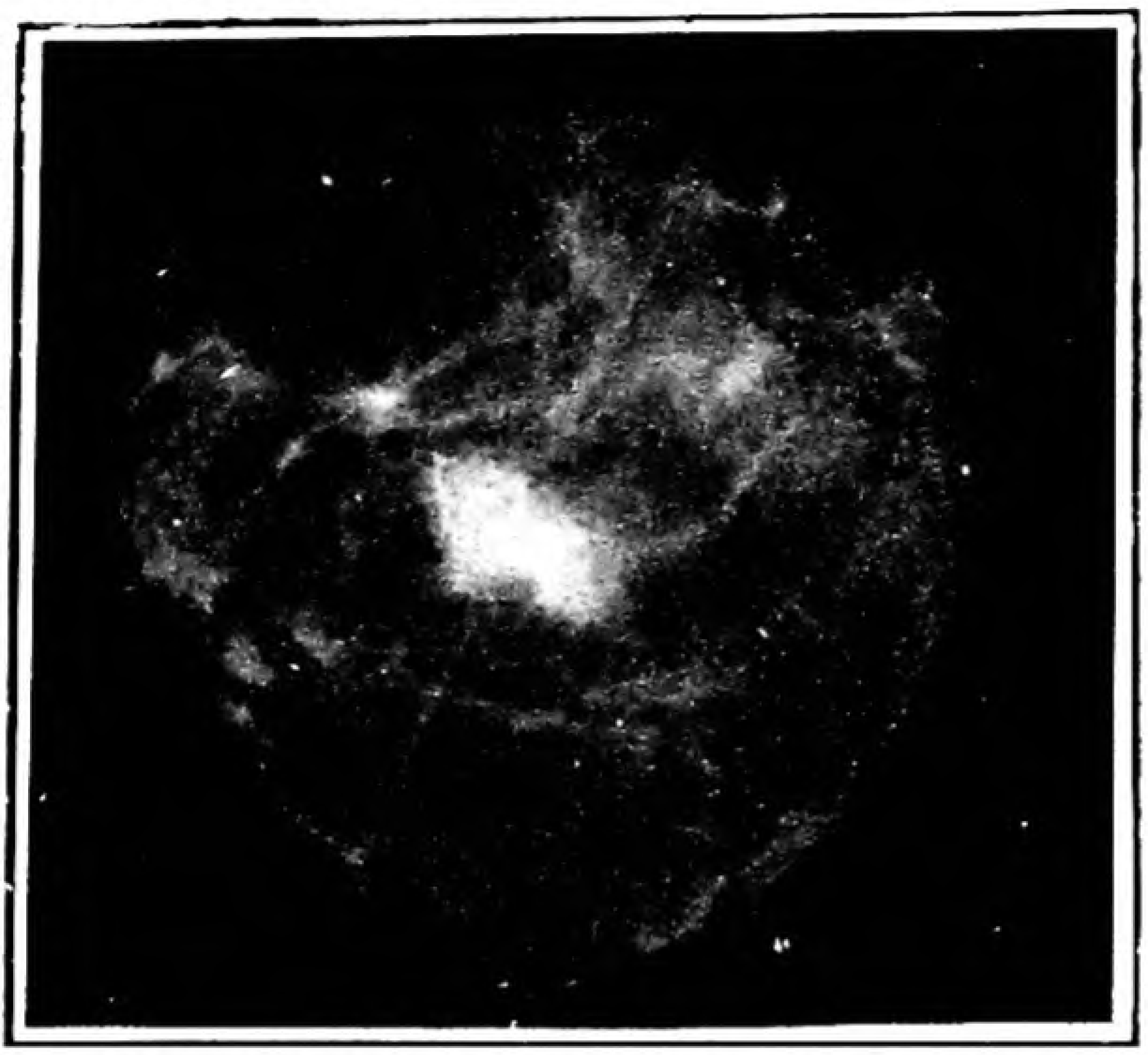

Fig.3. Surgical specimen radiograph includes the lesion (arrow).

Core biopsy of breast lesions can also be performed with ultrasound guidance. The advantages of ultrasound guided core biopsy are that it is faster, requires no radiation and the breast is not compressed. However, breast lesions which are not visible by ultrasound, such as those which consist of calcifications only, cannot be biopsied with this technique.

LIJ Experience

Since May 1991, stereotactic core biopsy was performed in 111 patients with mammographically suspicious, non-palpable breast lesions. 57 of these patients were participants of an ongoing study comparing the results of large core breast biopsy with open surgical biopsy under a protocol approved by the institutional review board and after informed consent was obtained. Mammographic abnormalities of this group consisted of a mass in 28, calcifications in 19 and both masses and calcifications in 10. After the needle core biopsy and the localization wire placement, these 57 patients underwent surgical biopsy.

The core biopsies were performed using a Mamotest Stereotactic System (Fischer Imaging, Denver, CO), Biopsy Gun (Bard Urological) and 14 guage core biopsy needle. The histo-pathologic findings from needle core biopsy and surgical excisional biopsy were reported by different pathologists. Tissue sufficient for histologic analysis was obtained from the stereotactic large core biopsy in all 57 patients. Pathologically there were 39 benign and 18 malignant lesions. There was complete agreement between needle core biopsy and excisional biopsy in 55 cases (96%). There was partial agreement in two cases. One case was diagnosed as atypical ductal hyperplasia by core biopsy and the pathologist advised surgical biopsy. The mammographic abnormality was a small cluster of microcalcifications. This case was in the early part of the study and only three cores were obtained. Surgical biopsy revealed intraductal carcinoma. In the second case, the mammographically detected abnormality was diagnosed to be a fibroadenoma both by core biopsy and surgical biopsy. However, there was a 0.4x0.5 cm infiltrating duct carcinoma in the specimen close to the surgical margin which did not produce any mammographic abnormality. Of the group who were referred for core biopsy only, two patients had lesions that were missed on previous surgical biopsies. Stereotactic core biopsy successfully yielded a definitive diagnosis in these two patients. (Fig. 3)

Our results are similar to those of Parker et al., who reported a series of 102 patients with an agreement rate of 96% between core biopsy and surgical biopsy. The core biopsy yielded a correct diagnosis in two cases that were missed at surgical biopsy; two lesions found at surgery were missed at core biopsy.

As a result of these studies, we believe that stereotactic automated large core biopsy of non-palpable breast lesions is an accurate and viable alternative to surgical excisional biopsy in appropriate cases. The advantages of stereotactic core biopsy over open surgical biopsy include elimination of the potential for complications and disfigurement, decreased time required for performing the procedure and decreased cost (25-50%). However, to ensure maximum benefit for the patient, a strict and proper protocol should be followed and a team approach between the radiologist, pathologist and the surgeon should be utilized for stereotactic core biopsy.

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LETTER TO THE EDITOR

Veracity In Medicine

The last two decades of the present Century have seen the emergence of some remarkable trends in medical practice. Treatment costs have increased tremendously, often they are beyond a patient's means, and so cost conservation for both the patient and the State has been the focus of attention world-wide. Young physicians today find themselves surrounded by influences such as evidence-based therapy, malpractice suits, quality assurance and very high technological standards. A physician in the United States needs to justify the investigations and/or treatment ordered for a patient, failure to do so results in non-payment for his services. A doctor in Britain must be able to explain why, for example, a chest X-ray was done or why it was not done if this would have benefited the patient, similarly, for the prescription of Cephalosporin or passing a scope into the urinary bladder. Much importance is given to unnecessary and unwanted hurt, be it physical or psychological, inflicted upon a patient or a patient's family. With diagnostic tools on which physicians have access today, the use of empirical therapy is not acceptable. Practitioners who overlook these important aspects of current medical practice invariably find themselves contestants in the courts of law.

It seems that physicians in our Valley have not been able to catch up with these concepts, hence a number of unjustifiable forms of medical practice are witnessed. Many such practices have been a personal experience, horrifying as well as worrying. The JK Practitioner is a good medium through which to draw the attention of my colleagues to a few simple, yet very vital, issues. In our part of the world too, the population of specialists is increasing. The physician who first sees the patient, and who may not be qualified or experienced enough to manage the condition, may refer the patient to the appropriate specialist. There should be no feeling of inferiority in making such a decision because it is in the best interest of the patient. In this way, a general surgeon will not manage a patient with hypertension of non-surgical cause, nor will a gastroenterologist look after a young lady who is depressed, she will be referred to a psychiatrist. An old man with no organic disease, just aches and pains here and there, needs reassuring; he most certainly does not need daily intramuscular injections of Voveron in a possibly fragile and atrophied buttock. This poor man would likely develop abscesses on both sides and go through misery to get rid of the infections. Add to the misery and the pain, the cost and inconvenience in obtaining the injections. We must ask ourselves, are we really helping this poor old man? It is completely unacceptable for a child of seven months to have twice-daily injections of Penicillin when his upper respiratory infection may equally well be treated with one from a large range of oral antibiotics that are readily available, even in remote market places. One finds, to ones utter amazement, scores of patients who have been on a number of medications for a long time, sometimes years, for a condition that was never accurately diagnosed, on the basis of diagnostic evidence. It makes one sad to see a very fit 26 year-old soccer player from a well-to-do family who is not deficient in food nor its absorption, on alternate-day injections of vitamins B1, B6 and B12. A typical prescription for a non-specific headache comprises an analgesic, a tranquilizer, an antiacid, a digestant and at times a beta blocker too, if the physician thinks he is a smarter one. There must be a multitude of comparable instances from different areas of medical practice. The purpose of this note, however, is not to highlight these, but rather to remind the medical community of their responsibilities. Medical practice means relieving a patient of an ailment and pain of possible, and alleviating the burden of care and concern on other member of the affected family. We are, unfortunately, doing the opposite. There is no justification in a physician taking upon himself the responsibility for treating anything and everything when he very well knows that this is not possible. This is not synonymous with help, on the contrary it could well compound the troubles for the patient and his family. The physician must not be swayed by the patient who believes he knows best and demands unreasonable treatment.

It is not my intention to preach medical ethics to my colleagues. If that were so, I would talk about the number of practitioners who treat the family of a fellow doctor, free of any charge. I do, however, wish to draw the attention of physicians to the malaise of litigation that has overtaken the West and is knocking on our doors too. It is just a question of time and of somebody being the first victim. With the returns for their services being as meagre as they are, physicians from the Valley can ill afford to lose a large portion of their income to medical defense agencies and the courts. This trend we can most certainly do without; once it starts it will get worse day by day. We must learn a lesson from the West, where things have got so completely out of hand that many young men and women do not find the medical profession an attractive one anymore. Strict quality assurance is the need of the times, and it falls to all physicians to mould themselves to the changing trends in medicine. Specialists, and teachers of medicine in particular, are expected to lead the way towards ensuring that medical practice is patient-oriented and based on evidence and not "instinct." The younger generation may find themselves coping with diffculties and a tense medical. practice unless they are guided on to the right path from the start.

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Jk-Practitioner 1998; 5(1): 77

OVERSEAS DIARY

Membership of the Royal College of Physicians - Viva Examination

M. Afzal Mir, *MB, DCH, FRCP.*

Most candidates with adequate knowledge required to pass the examination of the membership of the Royal College of Physicians (MRCP) consider the viva the easiest part of the test. This is only superficially true and sometimes brings forth a brutal surprise to those who have not properly prepared for it. The unlucky ones who do not pay enough attention to presentation are often left to lick their wounds after a bruising viva encounter. You may be clever and knowledgeable but the examiners do not know that unless you process their questions carefully, find the right information, support your arguments, and articulate your answers.

Although not as important as the short cases, the viva is an integral part of the MRCP examination. It is the only setting where the examiners get a chance to test your ability to deal with medical emergencies and referrals from within or outside the hospital, judge your communication skills, and explore your *knowledge* of topical and ethical issues. A candidate who creates a bad impression in any major area of clinical importance in the viva can fail the entire examination. The examiners will see to it if they suspect that the candidate is not capable of practising without supervision. This is an area where you can create a good impression and score a high mark rather than ruin whatever good you have done in other sections of the examination. Thus, the viva deserves the same consideration as the short cases and you should prepare for it and have mock exercises to sharpen your presentation.

Preparation

The best and most efficient way to accumulate knowledge is to read a standard textbook about each disease after you have seen a patient. The patient serves as a references or a `memory pillar' and reinforces your learning experience. This is also the time to learn abstraction; summarise the chief features of the condition to yourself as if you are facing an examiner or a medical audience in a clinical meeting. If you make a diagnosis ask yourself what is against it and how you would support your contention, and if you make a therapeutic decision ask yourself whether you would still make the same decision if the patient were to have its most serious side effect, and how you would defend yourself in a court of law. This approach allows one to develop sound clinical practice and prepares one for any encounter.

In addition to your usual textbook, the monthly *Medicine International* and *Hospital Update* series, you also need to read the editorials on the main medical topics in the three general journals, the *New England Journal of Medicine*, the *Lancet*, and the *British Medical Journal*. If you have not had access to any of these then find a library, when you are in the United Kingdom for the examination, and leaf through the recent issues. Take this opportunity to consult the *Prescribers' Journal* and the *Drug* and *Therapeutics Bulletin* which present up to date views on drugs and management strategies. You may also find it useful to read our book, an Aid to the MRCP Viva. From a few weeks before to the day of the examination watch the lay press for any news item of medical importance, such as a recent outbreak of an illness (e.g. meningitis, diarrhoea, etc.), or the relationship of benign spongiform encephalitis to Jakob-Creutzfeld disease. The examiners do not seem to appreciate the fact that you may have recently come the U.K. and may not have known what was grabbing the headlines in the British media.

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From the University of Wales College of Medicine Health Park, Cardiff CF 4 4XW UK

One examiner asked me something about a recent outbreak of Listeriosis and he wanted to know what I knew about it and what I thought was the source of it. The examiner did not look very impressed when I said that I'd only been in the country a week. I later discovered that this outbreak OF Listeriosis had been traced to contaminated soft cheese and there was a lot about it in the news papers. The other examiner with a broad grin chipped in, 'Can Salmonella be transmitted through an egg curry?" This was supposed to be a pun but it went completely above my head. I later learned that Mrs. Edwina Currie, a junior Health Minister, had created a furore by saying that all eggs carry Salmonella.

Consult a small book on emergency medicine and learn the management of common emergencies and poisonings. Testing the candidates' knowledge in emergency medicine is one of the main reasons for the retention of the viva in the MRCP examination, since the management of rapidly evolving situations cannot be adequately tested either in the short or the long case sections.

`Mock' viva practice

Arrange some `role-play' sessions with fellow candidates where you can ask each other questions on common emergency problems, such as status asthmaticus, acute gastrointestinal haemorrhage, paracetemol/aspirin poisoning, acute left ventricular failure, status epilepticus, and so on. Simulated sessions are important for improving one's ability to cope with the viva, and also sharpen one's presentation for the long and short cases examinations. It is particularly desirable to get someone who teaches for, or at least holds the, membership diploma. If such a person is a `hawk' and can put you a slippery surface, then the sessions can improve your spontaneity, sharpen your responses in answering questions, and can reveal your areas of deficiency and any unwelcome mannerisms, which may distract, or even annoy, the examiners.

Single `mock' exercises are useless unless you supplement these by a thoughtful and introspective analysis, and arrange further sessions in which you address your deficiencies. Invite criticisms after each session (better than failing the exam!) and try to improve your imperfections. This practice will stand you in good stead in every part of the examination. You will of course need a sturdy personality and a thick to benefit from these.

The viva examination

If you have properly prepared for the examination (it is a loss making exercise if you go unprepared!) then you should have no difficulty going with a positive appraoch, with the knowledge that the vast majority of questions are straight forward and the answers are well known to you. Even if the examiners ask you something about a rare condition there is no harm in admitting your ignorance. Candidates are known to have passed even they could not answer two questions in the viva. It is worth reminding yourself that the viva is not simple test for recall of information; rather the examiners' task is to test your ability to deal with clinical situations.

At the appointed time you will be ushered into a room where you will find two examiners ready to ask you questions. Enter gently, close the door and greet the examiners (Good morning/afternoon) as you would a senior colleague. Sit in the whole of the chair and not only on the edge (you will look nervous) and relax, but do not stretch your legs too far below the desk to dangle with those of the examiners. Before you sit down the examiners might stand and introduce themselves to you.

Make sure that you do not display any unnecessary kinetic behaviour (body language) as you sit down. Some people cannot avoid and are not aware of a rhythmic, tetanic, 1-3 flexions/contractions a second in one of their legs when they are sitting in a chair. If it is your habit then suppress it as it creates a bad impression on an examiner as it surely does on a patient. Similarly, if you are in the habit of displaying any other bodily movements try and suppress them.

Questions

Each examiner will ask you questions on two topics. However, the first examiner may try to lighten your burden by asking you a few informal questions about how things have gone so far or how you have fared in the short cases. This is simply an attempt at breaking the ice and do not go into a long discourse about how interesting your short cases were or how you enjoyed the examination! The examiner will usually describe a clinical scenario from his/her experience and will invite your comments. Always try to identify the examiner's concern and address it and do not get submerged in the story around the clinical problem:

You are in the Emergency Room and you see a Mr. Ali Baba who has been referred with a history of chest pains.

Ali Baba heads a huge firm of 40 accountants, he first developed a tightness across his chest when he was shouting at one of his accountants. That happened 3 days ago but he had further pains on walking, when he was answering a telephone call and last night when he was in bed. He got breathless and feels as if he is suffocating in a cave! How would you manage him?

It is easy to see that the underlying concern of the examiner is unstable angina and you need to address it without waffle:

The story suggests that Mr. Baba has unstable angina but I will need to exclude acute myocardial infraction by ECG and serial enzyme studies. I will admit him to the Coronary Care Unit where I can monitor his clinical state, ECG and cardiac enzymes. I will start him on an intravenous infusion of a nitrate, and administer heparin and give him aspirin.

Questions about common clinical problems do not leave much room for making mistakes; you should articulate your answers from a combination of your own exprience and knowledge. If the examiner gives a brief scenario try and build on it by making some reasonable assumptions without asking them many supplementary questions. Remember, you and not they are supposed to get a mark for answering questions.

After poor short cases I felt that I had to score a high mark in the viva so I tried not to let the examiners do any talking, since that would not have got me any marks! I started talking as soon as they had put a question using phrases like, 'Yes, well that is a crucial/key/important area', while I was thinking of the best reply. I think that practice in public speaking is important.

If the examiner raises a controversial issue (e.g. helath screening for all; euthanasia; digoxin in heart failure, CAT & MRI scanners, expensive but useless; etc.) then present both sides of the argument before giving a personal point of view. Always bear in mind that what might have been controversial when you started preparing for your membership examination may have become accepted clinical practice (e.g. anticoagulants in atrial fibrillation).

Just as in the other parts of the examination, the examiners do not give any feedback and do not offer any encouraging or discouraging remarks. Maintain eye contact with the examiner who has asked the question, and spare a few glances at the coexaminer who might give you an involuntary nod or a shake but do not depend on it.

Make a deliberate effort to keep your voice soft particularly when you know the answer very well and find it hard to contain yourself. In the excitement of the examination it is easy to lose control on your voice and shout your answer. While emphasising a point refrain from making a fist or banging on the desk. Such gestures look aggressive and raise tension. It is advisable to avoid all mannerisms which are likely to distract the examiners.

When the bell is rung and the examiners indicate the end of the viva, thank them and alight gently from your chair even if your experience was not very pleasant. As you leave the room be careful not to bang the door.

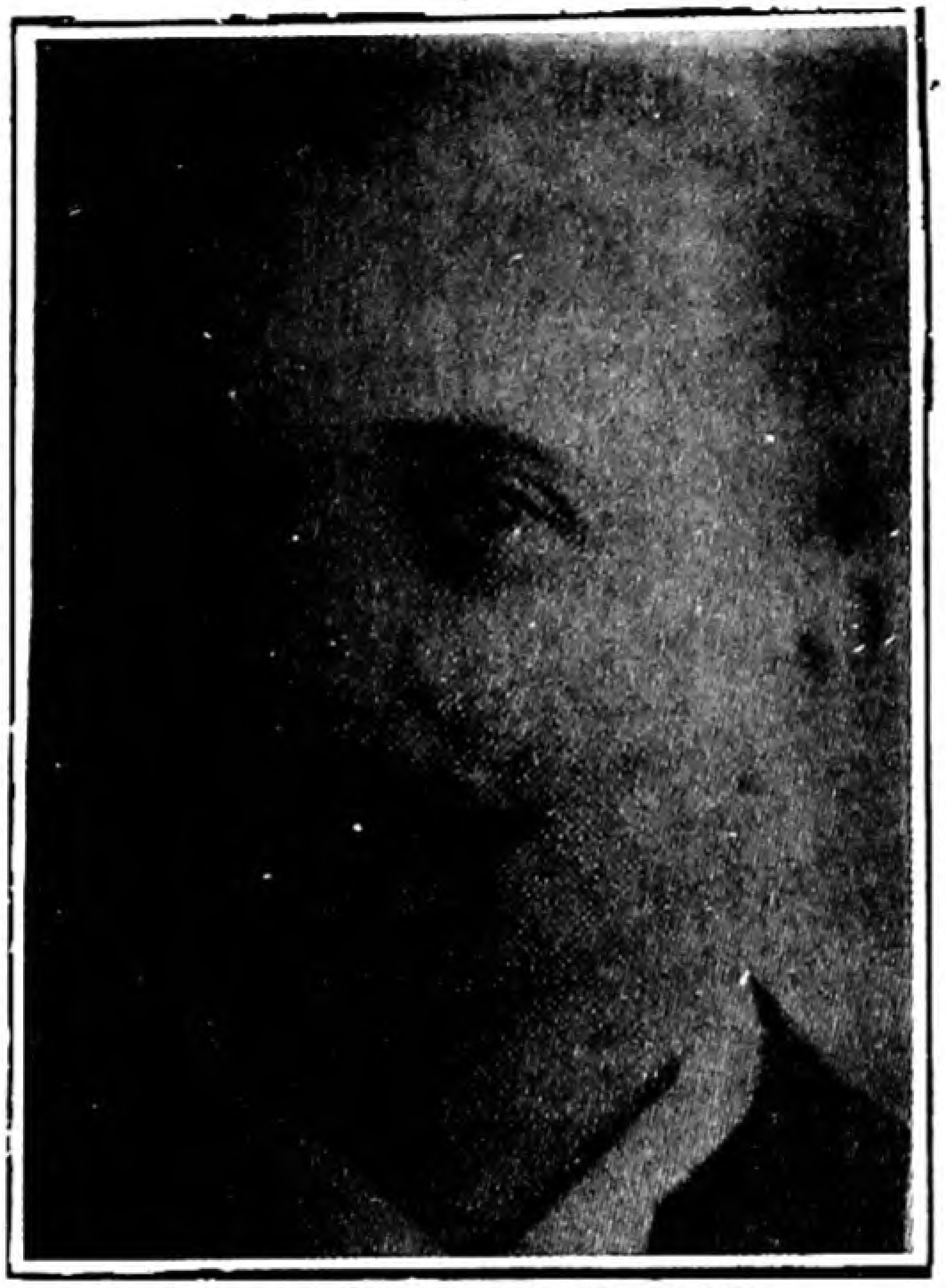
HISTORY

Aspirin-A Centenarian with a Difference

Zaffar Abbas Khatib, MD; Mushtaq Ahmad Shah, MD; Fayaz A Bhat, MD.

Galen's observation about old age as, "the driest time of life" or his pessimistic approach to life, "what after all, is old age other than the pathway to death?", may hold some substance is relation to human beings but not so with acetyl salicylic acid - a drug which attained hundred years of age in August 1997, shows no sign of death. In fact it is bouncing back to extended youth as vigorously as it had arrived one hundred years ago, with a new set of indications at the turn of this century.

The history of aspirin can be traced to 200 BC when the Greek physician Hippocrates prescribing extracts of willow bark for relieving pain associated with fever. Edward Stone (UK) is generally credited with the first scientific description and beneficial effects of willow bark in 1763. The active ingredient in the willow bark was first isolated in pure crystalline form in 1829 by a French pharmacist Henri Leroux, who also demonstrated its antipyretic effects. This active ingredient turned out to be a bitter glycoside called salicin. It was however, a Dundee physician, Thomas MacLagan (1876) who conducted the first proper clinical trial of the drug. He himself took 2 g of salicin and obtained complete remission of fever and joint inflammation without any ill effects. As the news of the beneficial effects of the extracts of willow bark spread, its demand rose. Herman Kolbe the professor of chemistry at Marburg University identified its chemial structure and was successful in synthesising it in 1859. By 1874 a factory at Dresden was producing it on a large scale and providing sodium salicylate to the people at tenth of the price of the material extracted from the willow bark.



Flex Hoffman (1868-1946)

The commercial production of salicylic acid made it available to a large section of the population but its unpleasant taste and stomach irritation were hurdles to overall patient acceptability. Here stepped in 29 year old Felix Hoffman, a chemist with Friedrich Bayer and Co, Elberfeld Germany who prompted to produce a better compound for his father, Herr Hoffman's rheumatoid arthritis, began experimenting with the phenolic groups of salicylic acid, was able to acetylate this group on 10th August, 1897 to obtain acetylsalicylic acid in pure form. This new compound proved to be superior in efficacy both as an anti-pyretic and anti-inflammatory with no unpleasant effects on the stomach. This was evident from both experimental and clinical studies carried out in Heinrich Dresser's (head of the pharmacology unit at Bayer's) laboratory and at Deoconess Hospital, Hale an der saale respectively. Incidently animal studies for an industrial drug was not known till then. Acetylsalicylic acid was registered under the name of Aspirin by Bayer. The "a" came from acetyl and spir came from the first part of spirea ulmania the plant from which salicylic acid had originally been isolated. With an excellent marketing strategy it was soon to become the number one drug, and Bayer's aspirin latter dispensed as water soluble

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tablets became an instant world-wide hit.

Dr. Lawrence Craven's observation in 400 patients that aspirin a day reduces the incidence of heart attacks was not accepted at first by the medical community in 1948. As its mechanism of action began to unfold many puzzles of its therapeutic benefits in cerebrovascular and cardiovascular diseases began to fall in place. John R Vane a British pharmacologist was awarded a Nobel Price for medicine in 1982 for telling us that aspirin acts by inhibiting prostaglandins. The FDA had given approval for the use of aspirin in 1982 for its use to reduce the risk of strokes in men. As the mystery around aspirin was unreaveled the FDA indications for its use also rose. In 1985 OK was granted for using aspirin in patients who had suffered previous heart attacks or angina. In 1996 it included patients suspected to have heart attacks. The US FDA'a signals were further broadened to include women for prop hylatic aspirin for prevention of strokes

In 1950 aspirin had earned a place in Guiness book of records a the most popular pain killer in the world. In 1969 the onboard firstaid cabinet of the Apollo 11 spaceship contained Bayer's aspirin-perhaps for Neil Armstrong to cool his head as he was to put the first step on moon. In USA about 35000 kg. Of aspirin is now consumed daily. The corresponding figure in UK is 6000 kgs. Weather it is the century old Bayer's aspirin or any other brand, aspirin accounts for more than 40% of almost $ 3 billion a year in retail sales of over the counter analgesics.

Aspirin is not likely to fade away. In the past 10 years or so its indications have been expanding and major trials are showing is efficacy as an anti-platelet agent, in prevention of myocardial infarction, stroke, migraine, dementia. At the end of this century there may yet be another approved use of this drug-reducing the risk of colorectal cancer. Dr. Sam Shapiro's (Boston University) hypothesis five years ago that bowel cancer may be prevented by regular use of aspirin may turn out to be correct. Some 15-20 studies conducted since then suggest that the risk of colon cancer reduction is between 30-50%. Dr. Sharpiro believes that aspirin interferes with the biochemical mechanisms that cause the cell lining the bowel to become cancerous, and this may involve prostaglandins. The stage is set for a new generation "superaspirins" to be used prophylactically in people at high risk of developing bowel cancer.

Unlike other old drugs aspirin is like to retain its blockbuster career well into the next century-retirement for aspirin is far far away-as it grows older its indications are increasing. This is really a centenarian with a difference.

Further Reading:

1. An aspirin a day keep the doctor at bay. The Eastern Pharmacist 1997; XL(478):27-28.
2. Elder DJE, et al. Are aspirin and other non steroidal anti-inflammatory drugs effective in the prevention and treatment of colorectal cancer? Lancet 1996; 348:484.
3. Featherstone C. Aspirin for bowel cancer: an old friend finds a new role. Lancet 1997; 350:418.
4. Insel PA. Analgesics anti-pyretics and anti-inflammatory agents: Drugs employed in the treatment of rheumatoid arthritis and gout. In:Hardma JG, Molinoff PB, Ruddon RN, Gilman AG. eds. Goodman and Gilman' The pharmacological basis of therapeutics. McGraw Hill 1996:617-618.
5. Jac DB. One hundred years of aspirin. Lancet 1997; 350:437-439.
6. Perimutter EM. Aspirin at 100. The Eastern Pharmacist 1997; XL(478):212-24.

JOURNAL SCAN

Aspiration verses Operation for Hepatic Hydatidosis

A prospective, randomised study of 50 patients of hepatic hydatidsis, was undertaken in Sheri-Kashmir Institute of Medical Sciences Sriangar.

25 patients were subjected to percutaneous drainage plus 8 wks of Albendazole therapy and 25 patients t cystectomy. Every patient in either group had clinical, biochemical, sonographic and serologic follow-up. The mean hospital stay was 4.2 ± 1.5 days in drainage group and 12.7 ± 6.5 days in the surgery group ($P<0.001$). The cysts disappeared in 22 patients (88 percent) in drainage group and in 18 (72%) in the surgery group ($P=0.29$). Anti body titers were negative in 76% in drainage group and 68% in the surgery group. There were procedure related complication in 8 patients (32%) in the drainage group and 21 (84%) in the surgery group. It is concluded that percutaneous drainage plus albendazole therapy is effective and safe alternative to surgery for treatment of uncomplicated hepatic hydatid cysts.

Khuroo MS, DM; Wani NA, MS; Gul Javid, Khan BA, MD; Yattoo GN MD; Shah AMD; Jeelani S, MD.
Percuntaneous drainage compared with surgery for hepatic hydatid cysts. N.Eng. J Med. 1977; 337:881-7

Endogenous Basic Fibroblast Growth Factor (bFGF) - Tumor Invasive Factor

The treatment and prognosis of any malignancy depends on invasiveness and spread of the malignant cells. Tumour spread remains a major challange in the treatment of the disease. Fibroblast Growth Factors (FGFs) hav been incriminated as potent mitogens, angiogenic agents and motogens. This study has used a cellular model in which two independently isolated series of colon carcinoma cells were developed, possessing different invasive potentials. BFGF and its receptors have been observed in normal and malignant colonic mucosa and in human colon carcinoma cells. Many studies, including this study carried out by Galzie Z etal has suggested a casual relationship between endogenous production of bFGF and invasive potential of human colon carcinoma cells.

The growth stimulatory and invasion promoting effects of bFGF were examined in these 2 series of related human colon carcinoma cell lines (HCT 116A, HCT 116 B AND 20-10-1 as well as LS 180, LSI 74T and ARKIA).

The invasive cell lines 20-10-1 and ARKIA grew more rapidly than their non-invasive counterparts by adding exogenously bFGF. The implication of these findings is that bFGF produced by carcinoma cells not only increases the growth rate of the cells but also stimulates their invasiveness, thus, the dual role of bFGF suggests that anti bFGF strategies could form the basis of a novel approach to the treatment of colon carcinoma.

Source: Zoya Galzie, David G. Fernig, John A. Smith, Graeme J. Poston and Anne R. Kinsella, Invasion of Human colorectal carcinoma cells is promoted by endogenuous basis Fibroblast growth factor Int J. Cancer; 1997; 71:390-395.

Functional Cast Bracing Superior to Other Conventional Methods in Treatment of Colle's Fracture

In managing colles fracture, the extent of plaster, technique of immobilization and position of band and the forearm in plaster have been points of controvery among orthopaedic surgeons. But functional cast bracing in supination effectively maintains the reduction of the colles fracture while at the same time allowing motion wrist. By eliminating the influence of the brachioradials muscle, which acts as a deforming force in colle's fracture, functional cast bracing in supination reduces the incidence of residual deformity. This technique allow early and complete return to normal function. It is cost efficient and can be applied at any orthopedic centre. This prospective study was done in 100 consecutive cases of Colle's fracture and none had poor functional results

GA Hagroo, T. Singh
Role of functional cast bracing in the Rx of Colle's fracture : Ann. Saudi Med. 1994; 14 (1); 37-41

Correlation of Iodine deficiency with Thyroid Malignancy

Iodine deficiency is known to cause thyroid hyperplasia, adenoma formation and ultimately malignancy in experimental animals. A study was undertaken at the S.K.I.M.S. to assess the prevalence of thyroid malignancy in Kashmir valley, an iodine deficient area. The study revealed a definite increase in relative prevalence of follicular carcinoma in Kashmir.

Source: Zarger A.H.; Laway B.A.; Masoodi S.R.; et al. Clinico-histopathological spectrum of thyroid malignancy from an Iodine Deficient Area (Kashmir Valley) 1997 (Aug); Ind J Surg: 197-204.

Meta-analysis says Physicians don't listen to patients well enough

Physicians do not listen to their patients enough or give them enough information, according to the authors of this meta-analysis from Montreal. In one study of physician-patient interviews, patients spoke for an average of only 18 seconds before they were interupted by the physicians. Only 1 of 52 patients who were interupted, voiced and additional concern. Another study found that physicians underestimated their patients desire for information in 65% of cases of cases and significantly over-estimated the amount of time. They spent giving information. According to the authors, female physicians spend more time with their patients, give and seek more information and engage in more partnership building. Male physicians are more likely to make statements imposing their views and are more directive at the end of a visit.

The authors offer four suggestions for improving communication.

(1) Let patients finish telling you why they visited you.
(2) Solicit their views on the influence of psychological factors.
(3) Ask them what information they need from you.
(4) Make sure that they understand what was communicated.

Source: Rosenberg EE et al. Lessons for clinicians from physician-patient communication literature. Arch Fam Med 1997; 6: 279-83

Iodine Deficiency and Goiter

Endemic goiter and endemic cretinism continue to be impediments to an improved quality of life in many parts of developing world. Endemic goiter is widely prevalent in the countries of South-East Asia, the Himalayan endemic belt being one of the world's most extensive and severe endemic area. An extensive goiter survey in school children was carried out in Srinagar District of Kashmir Valley.

A total of 2017 school children were surveyed in the age group of 5-15 years, including 1118 boys and 899 girls. Overall prevalence of goiter was 33.75% carrying iodine estimation in 49 urine samples among surveyed subjects revealed mean ± SEM Urinary iodine, of 57.57±2.61 micrograms per gram of creatinine.

Source: Zargar AH, Shah JA, Laway BA, Masoodi SR et al. JIMSA, 1997; 10:44-50

BOOK REVIEWS

Handbook of Medical Emergencies and therapeutics. Mohd. Yousuf, 1997. Rs.: 110. Available at Ali Mohd and Sons Lal Chowk Sriangar

I must congratulate Dr. Yousuf for producing this excellent book which I am sure, will be useful not only for under-graduate and post-graduate students but to faculty members as well as to Medical Practitioners also.

Dr. G.Q. Allaqaband
FRCP
Ex. HOD Medicine,
Principal/Dean
Govt. Medical College Srinagar

Prof. Mohd. Yousuf deserves full credit for writing the book on Medical Emergencies. This book serves as a concise, authoritative summary of current treatment of a broad spectrum of illnesses in a distillate manner. The author has gone to a considerable extent in simplifying the interpretation of different modalities of treatment approach and quick diagnosis. I hope that this book will gain popularity among under graduate, post graduate and practitioners.

Dr. G.M. Malik
Department of Medicine

A dictionary of Medical Syndromes by Dr. Azra Shah. Valley Book House, Srinagar Kashmir 1997. Pp. 118. Rs. 310. ISBN 81-86592-04-0.

It is interesting to go through this book. With syndrome complex it is covering whole of medicine. It will be great help to post graduate students in brushing up their knowledge of medicine at a glance.

Prof. S.Z. Mehdi
MRCP
Deptt. of Medicine,
GMC, Srinagar

Postgraduate Medicine B.C.Bansal. Volume II 1997, available with the Association of Physicians of India 90, Sector 51-A, Noida - 20130.

This book by Prof. B.C.Bansal president API(1997) provides wide vision of academic Medicine and includes several topics on Neurology, Haematology, GIT, Cardiology, Endocrinology and Infectious diseases, Nephrology and other specialities. The book provides a complete update on various topics/diseases prevalent in this sub continent. I would recommend this book for every Clinician, Teacher and Post-graduate Students for them to keep pace with changes in Medicine. It includes papers presented during annual meeting of Association of Physicians India (API) 1997. The cost of book is reasonable and quality of papers is good. It will be helpful to have some diagnostic and imaging photographs in future additions.

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MEET THE PROFESSOR

Hamid Ali Khan Durrani
76 Indranagar, Sonwarbagh,
Srinagar, J&K, 190004

Date of Birth : March 7, 1934

Place of Birth : Basti, Uttar Pradesh

Academic Qualification:
MBBS (1956)
MD (1960) Internal Medicine, both from King George's Medical College, University of Lucknow, UP, India
FACG (1980) American College of Gastroenterology

Appointments :
Asstt. Professor (1965-81)
Associate Professor (1981-83)
Professor (1983-92) and Chief of Gastroenterology, Department of Medicine, Govt. Medical College Srinagar
Professor and Head of Medicine (1992 till date) JV College of Medical Sciences, Srinagar

Publications/Research:
About 20 publications in National and International Journals.
Guided about 12 research programmes

Membership of Professional Organisations:
Life member Indian Society of Gastroenterology
Life member, Society of GI Endoscopy of India
Member American College of Physicians (1980s)
President, GI Cancer Foundation of Kashmir 1997

Honours/Awards:
ICMR Fellow in Gastroenterology, AIIMS, New Delhi, 1970
Colombo Plan Fellow in Gastroenterology at Toronto Western Hospital, Toronto, Canada (1971-72)
Fellow in GI Endoscopy, Juntendo University Tokyo, Japan (1975)
WHO Fellow in Medical Education and Gastroenterology at the University of Toronto, Canada, Chicago, Illinois, and South California, Los Angeles (1977-78)
Special GI training courses at Mayo Clinic, Rochester (1972), Dallas, Texas (1978) Miami, Florida (1978).

Special Interests :
My Family : Massarat Durrani, Gynecologist
Afshan, Fashion Designer, Husband Nusrat Durrani, Business Executive, based at New York.
Zeba, Engineer, MBA, Husband Ayaz Siraj, Business Management, based Virginia, USA.
Sarfraz, MD, Chief Resident, Internist Nassau County Hospital, New York

Q & A's:

Q You have been an eminent physician of Kashmir, having a special interest in gastroenterology. What do you think are the areas of concern in relation to the Kashmiri population?

A Our published data and experience at the Govt. Medical College and Tender Mercies Gastroenterology during the past 25 years points to high prevelance rate of Gastric and Esophageal Carcinoma, accounting for approximately 46% and 43% respectively of all GI malignancies

Q The remedy?

A The GI Cancer Foundation of Kashmir, formed in October 1997, is aimed to provide directive and remedial measures by way of efforts to make early diagnosis, standardise medical and surgical therapy and identification of possible etiological factors.

Q How do you compare medical education in your time with the present system?

A The approach of bedside clinical diagnosis should never be lost in the midst of computer and scan age.

the former should remain the sheet anchor of medical care in our setting of the third World countries. What percentage of our population can afford total dependance on such diagnostic tests? and what percentage of medical graduates will have access to them?

Q What about the future?

A While superspecialisation contributes to ultimate medical care, the Internist approach should always remain.

Q Your views on (i) private medical education (ii) private practice by government doctors (iii) overall health services in J&K State.

A (i) Plethora of Medical Schools, sometimes run in small hired buildings, if allowed to grow, will undermine the standards of Medical Education which will adversely affect patient care. Such attempts should specially be prohibited in our State of Jammu and Kashmir.

(ii) Private Practice not linked to Hospital based patients and not encouraching on Hospital hours, may be permissable. Senior clinicians have shown the way, how practising Faculty Staff can also be good teachers and their practice never interferes or mixes with care of Hospital patients.

(iii) The J&K Health Services are at par, if not better, than the services in the rest of country. The need of the hour is to produce conscienuous, intelligent, competent and humane medical graduates, and the onus lies on the premiere Medical School of Srinagar.

Q What has given you the most satisfaction in your service career?

A My Students, their enthusiasm in my Lectures and bedside clinical teaching. That the GMC graduates have achieved laurels in India and abroad, is the satisfaction, where look back.

Q Disappointments.

A The sadistic beareucracy, wish our Medical School was totally independent run by the University, no red tapes I mean.

Q Regrets.

A Can I go back to mid sixties and restart teaching?

Q Your advice to young medical graduates.

A You are next to none, strive hard, donot lose sincerity and you will be on the top, where-ever you are.

Q Few words for JK-Practitioners present and future objects.

A As of today the JK-Practitioner has made its mark at national and international level. The standards of the articles should never be compromised at any time. The inside printing and paper can be further improved.

Q Which of your collegues in Medical Colleges have impressed you as a clinician, teacher or otherwise?

A All, I have enjoyed being part of the Faculty.

Q What are your near goals after retirement in the field of gastroenterology or social work?

A Cancer Foundation of Kashmir has been in my mind for quite sometime. With the interest shown by colleagues, it has come into being. I hope to devote time to achieve the goals set by the Foundation. Of course teaching is a flair for me, I have an assignment towards that. There are about one dozen Fellows of the American College of Gasfroenterology in India. I am planning to organize Annual Meetings of the Fellows for exchange of ideas and data, in the superspeciality of Gastroenterology. Hopefully the first meet will take place in Srinagar in the Summer of 1998.

NEWS

1. **Dr. M.R. Kotwal** MD, FACG; has been elected governor of the American College of Gastroenterology, Indian Region, for a period of two years. Dr. Kotwal completed his post-graduation in medicine in 1977 from Medical College Srinagar, Kashmir.
2. **Prof. Azra Shah** has been awarded fellowship of the Indian College of Pathology. She is the first person from the State of Jammu and Kashmir to be bestowed with this honour. At present Prof. Azra Shah is the Head of the Pathology and Microbiology department at SK Institute of Medical Sciences, Soura.
3. **Recent CME Programmes held in Srinagar**
   - A symposium on Corenory artery disease organised under the auspicious of Indian College of Cardiology on 14th October at Convention Complex was sponsored by Torrent.
   - Symposium of H.Pylori and GIT diseases organised by the GIT division of Govt. Medical College Srinagar at the GIT Deptt. of SKIMS, was held on 14 Dec. 1997 at the SK Convention Complex. The symposium was sponsored by US VITAMINS.
   - A symposium organised by the GIT Division Govt. Medical College Srinagar and JK-Practitioner was held at the Medical College ~~and~~ held on 16-12-97. (courtesy Hoechst Ltd.)
     Topic - Endoscopic diagnosis and Management of GIT Bleed.
   - A update on Hepatitis B at SKICC organised by GIT Division Govt. Medical College Srinagar, held Nov. 1997 & was sponsored by SKF Pharmaceuticals.
   - Symposium on AIDS awareness and Rational drug use, in Kashmir was organised by the Obst. and Gynaecology Deptt. of Govt Medical College Srinagar in collaboration with the voluntary health organisation of India, was held on Ist December 1997 at Lal-Ded Hospital Srinagar.
4. **Conference Calender**
   - **Conference on Advances in Clinical Pharmacology, 1 and 2 February 1998** and workshop on Basics of Clinical Pharmacology, 3 February 1998, organised by the Department of Clinical Pharmacology, K.E.M. Hospital, at Mumbai. For details contact Dr. N.A. Kshirsagar, conference secretariat, Department of Clinical Pharmacology, K.E.M. Hospital, Parel, Mumbai 400012.
   - **4th National Congress on Assisted Reproductive Technology and Advances in Infertility Management, 19 to 22 February** at Chennai. For details and registration contact the organising secretary, Dr. Kamala Selvaraj, G.G. Hospital, 6-E, Nungambakkam High Road, Chennai 600034.
   - **Fourteenth Temporal Bone Surgical Dissection course and Microsurgery of Ear and Larynx course, organised by department of ENT, LTMG Hospital, 24 to 28 February 1998** at Mumbai. For details contact Dr. R.A. Bradoo, Mohan Niwas, Dr. C.G.Road, Chembur, Mumbai 400074.
   - **Fifth International Congress on Cardio-Pulmonary Diseases organised by International Academy of Chest Physicians and Surgeons of the American College of Chest Physicians, East India Chapter, 27 February to 1 March 1998** at Calcutta. Contact the organising secretary, Dr. P.Dinda, Eko X-Ray and Imaging Institute, 54, J.L.Nehru Road, Calcutta 700071.
   - **XXXVII annual conference of College of Chest Physicians (India) - NACCON '98, 6 to 8 March 1998** at Indore. Contact the organising secretary, Dr. Sushil Mandovra, Chest & Allergy Clinic, 53, Prince Yeshwant Road, Indore 452004.
   - **3rd annual conference of the American College of Surgeons - India Chapter, 7 and 8 March 1998** at Ludhiana. For further details contact Dr. Kim Mammen, Department of Urology, Christian Medical College and Hospital, Ludhiana 141008.
   - **International Conference on Reproductive Health, organised by the Institute for Research in Reproduction, 15 to 19 March 1998** at Mumbai. For further details contact Dr. Chander P. Puri, deputy director, Institute for Research in Reproduction (ICMR), Parel, Mumbai 400012.
   - **Workshop on Advanced Hepatobiliary Surgery, New Delhi, India 14-15 February 1998.** Information: G.K. Pande, Department of G.I. Surgery and Liver Transplantation, All India Insitute of Medical Sciences, Room 1002, PC Block, New Delhi 110029, India.
   - **National Update on Asthma, Indian Asthma Care Society, Jaipur, Rajasthan, India 15-16 February 1998.** Information : Virendra Singh, C-86 Shastri Nagar, Jaipur 302016, Rajasthan, India.

Information for Authors

JK-Practitioner will consider for publication any material that advances the cause of Medical Science or practice through Clinical Medicine is its central theme. JK Practitioner also publishes basic science papers with clear clinical implications.

Intending authors shall submit their manuscripts to Dr. G.M. Malik, Editor in Chief. P.O. Box No. 884 G.P.O. Srinagar 190001 J&K (India).

Manuscripts are received with the understanding that they have not been submitted to other journals or News media. JK Practitioner is not responsible in the event that any manuscript is lost. Manuscripts become the permanent property of JK Practitioner if accepted and may not be published elsewhere, without written permission from the author and the journal.

Form of Manuscripts: Manuscripts written in english should be typed on standard white bond paper with margins of at least 25mm (1in). Type only on one side of the paper. Use double spacing throughout including title page, abstract, text, acknowledgement, references, tables and legends for illustrations. Begin each of the following sections on separate pages; title page, abstract and key words, text, acknowledgements, references, individual tables and legends. All pages beginning with the title page must be numbered consecutively. Both the form and the content of the manuscript should be carefully checked to avoid the need for correction in proof. Send three such copies. **The journal strongly encourage authors to submit electronically prepared manuscripts in wordstar or pagemaker (readymade) software packages on diskettes labelled properly.** Following the instructions set forth here exactly if, for example the reference section is incorrectly styled, the value of the diskette submission will be reduced. A double space hard copy of the manuscript must accompany the files copied on to the diskette.

Authors: All persons designated as authors should qualify for authorship. Each author should have participated sufficiently in the work to take public responsibility for the content. Designate one author as correspondent and Editor in Chief may require authors to justify the assignment of authorship.

Abstract: The second page should carry on abstract of not more than 200 words. The abstract should state the purpose of the study or investigation, basic procedures, selection of study subjects or experimental analysis, observational and analytical methods, main findings and principal conclusions. Abstract for case reports should not exceed 50 words. Do not use structured format. Abstracts are not required for editorials, reviews and special features of the journal.

Key words: Below the abstract provide and identify as such three to 10 key words or short phrases that will assist indexers in cross indexing the article and reflect the content of your manuscript. Use terms from the Medical subject headings (MeSH) list of index Medicus.

Text: The text of observational and experimental articles should usually but not necessarily be divided into sections with headings - introduction, methods, results and discussion. Long articles may need sub headings within some section to clarify their content, especially the results and discussion sections. Other type of articles such as reviews, editorials, guest articles are likely to need other formats. When in doubt authors should consult the latest issue of the journal.

Acknowledgements: One or more statements should specify:-
a) Contributions that need acknowledging but do not justify authorship.
b) Acknowledgements of technical help.
c) Acknowledgements of financial and material support.
This should be placed as a footnote at the end of the article before the references.

References: These should be cited consecutively in the order in which they are first mentioned in the text as superscript numerals and listed on a separate sheet in numerical order. References cited only in tables or in legends to figures should be numbered in accordance with the sequence established by the first identification in the text of the particular table or illustration. Each reference should contain in order the following:-

Author (last name initials) title of the article, source, year of publication, volume and inclusive page numbers. Abbreviation of journal name should conform to Index Medicus style. Examples of correct form of reference are given below:-

Journal article

1. Riggs BL, Seeman E, Hodgson SF, Traves DR, O'Fallon WM. Effect of the floride/calcium regimen on vertebral fracture occurance in Postmenopausal Osteoporosis. N. Engl J Med 1982; 306:446-50.

Book

2. Saldana MJ. ed. Pathology of Pulmonary disease. Philadelphia, JB lippincott company, 1994; 203.

Book Chapter

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EDITORIALS

Free Radicals and Cancer

The incidence of cancer is largely conditioned by nutrition and dietary factors seem responsible for 30-40% of all cancers. Dietary nutrients affect body's physiology, both promoting and preventing cancer development. Endogenously generated and xenobiotic electrophilic toxins or their metabolites are significant contributors to the age related genomic senescence, which may trigger 'Apoptosis' (stereotypic programmed cell death) or alternatively an abnormally dangerous pathway involving regulation of expression of genes involved in controlling growth rate, mitosis, DNA damage recognition or DNA repair and cell differentiation eventually result in malignant phenotype having unregulated growth rate, genetic instability and clonal selection resulting in a cell population capable of inducing vascular growths within the tumor, invasion of surrounding tissues and propensity of dissemination through vascular and lymphatic routes.

Free Radicals are highly reactive independant molecules having one or more orbital electrons contrast to the biological molecules having paired electrons. Free radicals are superscribed by a dot (H;OH, O_2). Free radicals have potential to oxidise biological molecules (proteins, lipids, calcium, DNA) and it is estimated that DNA in each cell of human body receives about 10,000 hits per day. Oxidative stress is a term used as an index of prevalence of oxidising species within a system. Electron rich bases of DNA are susceptible to the mutations as a result of electrophilic attack by strongly electrophilic species (oxidising chemicals) capable of abstracting electrons and by weaker electrophiles (capable of adduct formation through substitution reaction). The electrophilic stress is more appropiate in the context of theories stating that accumulation of mutations in DNA is a major contributor to the carcinogenesis. Compounds such as: 1) Reactive oxygen species (ROS) formed as byproducts of aerobic respiration from mitochondria, peroxisomes, electron transport chains of endoplasmic reticulum or cyclic oxidation or reduction of endo or exogenous quinones., 2) electrophilic or oxidising metabolites of hydrophobic endo or xenobiotics during phase I metaboliasm by the cytochrome P-450 systems., or 3) Reactive intermediates of intermediary metabolism such as alpha and beta unsaturated aldehydes are the primary sources of the electrophilic stress that must be guarded against to prevent mutagenesis. ROS including hydroxyl radicals, perhydroxyl radicals, superoxide anion, hydrogen peroxide and singlet oxygen probably represent the major endogenous oxidants. Physiologic, toxic or infectious events leading to the increased generation of ROS or non-oxygen oxidants or electrophiles can lead to increased rate of accumulation of mutations in DNA. Electron leakage in the mitochondria is the major source of endogenous oxidative stress in the form of superoxide anions and hydrogen peroxide. Aproximately 2% of daily oxygen consumption by the mitochondria results in the formation of superoxides and hydrogen peroxide. Few cellular targets are susceptible to the significant damage by these two species. Fe^{+++} can use hydrogen peroxide to produce extremely toxic radicals through Fenton Reaction and the super-oxide anion can then be recycled to the Fe^{+++} to Fe^{++}. The one electron reduction potential of hydroxyl is sufficiently high to oxidise membrane lipids (L*) resulting in the formation of lipid alkyl radicals (L*) in fatty acids which are converted to an alkyl peroxy radical (LOO*) by combining with oxygen and subsequently to a lipid peroxide (LOOH). Fe^{++} can reduce lipid peroxides to alkoxyl radicals (LO*) and superoxide anions can accelerate this process by reducing this process by reducing the resultant Fe^{+++} to Fe^{++}. Alternatively Fe^{++} can oxidise lipid hydroxy peroxides to alkyl peroxy radicals. Lipid peroxidation can also yield the mutagenic ROS, singlet oxygen and other radicals. Polymorphonuclear cells and macrophages in the sites of chronic inflammation also generate highly oxidising hypochlorous acid having a role in the endogenous oxidative stress in the chronic inflammation. Indeed, within the third world, where chronic infection by viruses and protozoans are a leading risk of cancer, chronic inflammatory processes represent a significant endogenous source of mutagenic oxidative stress. Xenobiotic like anthraquinones generate ROS through redox-cycling. Oxides of nitrogen present in cigarette smoke and nitrites present in certain foods can form oxidising nitros compounds, which have been strongly implicated in the carcinogenesis.

Eversince pioneering Wattenberg's, group studies showing retardation of Benzo (a) pyrene induced neoplasia in lung and fore-stomach of mice by the dietary anti-oxidants, a search for naturally occuring-synthetic anti-oxidants which would intercept the interaction of the ultimate carcinogens with DNA was made. The inhibition of carcinogenesis by these chemopreventive agents though exactly unknown is believed to be due to the detoxification of free radical scavengers, modulation of activation of the pro-carcinogens and more importantly th induction of anti-oxidant defense system enzymes.

Till recent, a balanket protection by anti-oxidant therapy in humans has been acclaimed by the scores of epidemiological studies. However, of late, two important studies (US Physicians Health Study and Beta carotene and Retinol efficacy trial CARET) involving 40,000 subjects put these hopes to rest and instead these researchers recognised an elevated risk of death from lung cancer in the group receiving supplements. These disappointing results of clinical trials re-affirm the importance of solid scientific knowledge as the basis for cancer preventing strategies. Probably these anti-oxidants (Chemopreventive agents) may not account for all the benefits with this dietary pattern and the myraid of other substances in plants, vegetables and fruits need to be examined for cancer preventive properties. There is need for sound scientific reasons to identify the true mechanisms underlying the epidemiological observations and to validate there importance in clinical trails.

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Noise Pollution: The Bane of Urban Living

Noise is one of the environmental pollutants that is encountered by the population in day to day life. It is creating health hazards and interferes with speech communication. Continued exposure to high levels of noise results in annoyance, fatigue and temporary shift of hearing which may lead to permanent noise exposure, causes physiological disturbances namely changes in digestion, metabolism and blood circulation etc.

In spite of this accuring evidence, though a lot of attention has been given to air pollution, water pollution and environmental pollution in general, there is hardly a voice against noise pollution. Victor Gruem had said "Noise is the slow agent of death."

In the developed world, large amounts of compensations are paid every year by the industry for occupation related hearing loss. In US alone, according to conservative estimates, noise induced hearing loss (NIHL) affects nearly 35 million Americans and industrial compensation to the tune of 20 billion dollars is paid for such occupational NIHL thus making hearing loss as the number one medicolegal and environmental problems in USA.

India is rapidly getting industrialised and in the process unplanned urbanisation has become a problem. Though no authentic study regarding the magnitude of problem exists in India. The urban Indian is exposed to a variety of noises both Industrial and non-Industrial. The higher noise levels in residential areas are mainly due to unruly traffic and in colonies situated near airports due to the aeroplane noise. As many so-called posh colonies are located in these areas the noise levels in the posh colonies is higher due both to the vehicular and other noise. The noise levels in middle income group colonies is lower as compared to the higher income group colonies where air conditions also add to the noise levels in the atmosphere. An aeroplane passing overhead can make a peak noise of 110 dB. A study by the Indian Institute of Road Traffic Education recently reported that Delhi is the noisiest city in India, followed by Calcutta, Bombay and Madras.

Exposure to noise induces many physiological and psychological changes. A study conducted by Defence Institute of Physiology & Allied Sciences revealed that high intensity noise not only affects hearing but also has adverse affect on the cognitive and psychomotor functions. Exposure to loud sound can cause reduction in the quality of life, loss of social well being, as the noise acts as a biological stressor. It leads to sustained activation of autonomic nervous system and hormonal imbalance causing various problems like hypertension, peptic ulcer, emotional unrest, tinnitus, fatigue, insomnia, mental depression, decreased concentration and decline in the work efficiency. It is predicted that if there is continued exposure to noise of 50 dB intensity everyday, most people in urban areas would be, hearing impaired by the year 2000.

Noise induced hearing loss is caused by temporary threshold shift in early stages leading to permanent threshold shift in case of prolonged exposure in a steady state for 10-15 years. Specific non-industrial noise hazards are:

1 Gunshots which cause a temporary threshold shift. There may be asymmetrical hearing loss.
2 Socioacusis is the hearing loss as the cumulative effect of prolonged social noise exposure.
3 Recreational noise exposure is caused by fireworks, model aeroplanes, snowmobiles, sport activities like motorcycle racing, boxing etc.
4 Aircraft noises.
5 Community noises like loud speaker noise of 'Bhajan Keertan', marriages and parties.

In short the urban atmosphere is bombarded by loud sound of vehicular traffic, loudspeaker, factory and aircraft, outdoors and indoors by music systems, radios, TV's, grinders, vacuum cleaners, electric pumps and also loud talking individuals.

The different levels of the sound can be measured by the Sound Pressure Label (SPL) metre on dBA or by the Audiodosimetre which shows the percentage of exposure. The nature of the early hearing loss is known as the Temporary Threshold Shift (TTS), followed by Permanent Threshold Shift (PTS), when a characteristic notch at 4 KHz is found on the puretone audiogram which is diagnostic of noise trauma. A sudden burst of very loud sound of 90 dB or more is sufficient to produce either rupture of tympanic membrane or even dislocation of the ossicular chain and sudden sensorineural hearing loss (SNHL). The maximum limit of noise specification for indoor spaces are as follows:

Residences Rural	25 dBA
Semiurban	30 dBA
Urban	35 dBA
Industrial	40 dBA
Hospital	30 to 40 dBA
Office	25 to 40 dBA
Auditorium	40 to 50 dBA
Restaurants	40 to 50 dBA

Hearing loss is one of the most challenging problems confronting medicine which can even affect the personality so adversely. A mild hearing loss sometimes may produce more psychological trauma than severe hearing deficit. The emotional effect of the hearing loss is sometimes more traumatic than the actual deafness as the hearing loss may sometimes bother the people around, more than it does to the patient. Deafness is rather a strange symptom as it is usually not accompanied by pain, discomfort or fear as in cancer or such other disease that compels the patient to seek medical aid. Is there a solution to this man made malady of noise pollution? Of course, yes, and the solution is by prevention and control of noise which can be done by various methods. The most effective measures are by reduction of the radiated noise, vibration damping, vibration isolation, noise barriers and enclosures, noise absorption, personal protection devices like pluge, insert, canal cap etc. An essential component of hearing conservation programme is audiometric testing and noise measurement. This latrogenic problem can also be prevented by implementing proper legal measures, health education and planning like not to construct school, hospital and residential colony by the side of road, railway tract or airport etc. Punitive action should be taken against the industries which violate the law regarding noise pollution. Professional societies and Indian Society of Otology (ISO) etc. should organize symposiums/workshops/seminars in collaboration with the Ministry of Health to create awareness regarding this menacing problem. Like other disease control programmes, a National Noise Control Programme should be started on which different non-governmental organizations (NGO) may be involved. In U.S.A., people are so much conscious of the danger of noise pollution that many communities have organized their own advisory councils to help them to fight noise pollution. But in India, where noise related problems are worse, we still do not make any noise regarding "Noise Pollution" till now. Silence is not always the best language!!!

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VP Venkatachalam, is the editor Chief of the Journal of Safdarjang Hospita, New Delhi and this Editorial has appeared in that journal (vol. 5, Number 1-4, 1997 pg. 5-6) and is reproduced here with permission.

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REVIEW ARTICLE

NSAID-Induced Gastric Injury

David Y. Graham

More than 30 million people consume NSAIDs each day worldwide[1]. In 1991, more than 70 million prescriptions for NSAIDs were filled in the United States. The per capita consumption of NSAIDs averaged 278 prescriptions per 1,000 population with ibuprofen and naproxen being prescribed most commonly.[2] The acutal use of NSAIDs was higher than the volume of NSAID prescriptions because it also included over-the counter use of aspirin or ibuprofen. Since 1991 two additional NSAIDs, naproxen and ketoprofen, have become available for over-the-counter use. Ketoprofen use may be associated with a higher risk of complications than ibuprofen and the United States may see a further increase in NSAID complications.[3,4]

Despite the progress in the diagnosis and treatment of H. Pylori-related peptic ulcer disease, it has become apparent that we may be in the midst of an epidemic of nonsteroidal anti-inflammatory drug ulcers and ulcer complications[5]. For example, it has been estimated that in the United States there are more than 75,000 hospitalisations and more than 7,500 deaths annually in the elderly directly related to NSAIDs.[6] The increasingly wide-spread use of NSAIDs has brought the problem of NSAIDs has brought the problem of NSAID associated upper gastrointestinal bleeding, perforation, and obstruction into sharper focus.

How Dangerous are NSAID's

Several studies have now shown that the risk of developing a serious, life-threatening ulcer complication is in the range of 1.3% to 2% of a population of NSAID users per year of Use[6,8]. Class labelling from the Food and Drug Administration tells physicians that the range is 2% of 4% per year. To put this into perspective, if the risk of having a major life-threatening automobile accident per year was 2% with 8% to 10% of those having an accident dying, one might look at alternate forms of transportation.

Can we replace NSAIDs? Patients take NSAIDs because of the tremendous benefits they receive in terms of pain relief and increased mobility[5]. We can minimize the risk by identifying patients at higher risk for developing complications. Some of the risk factors include advanced age, major comorbid disease, concurrent steroid use, past history of ulcer, ulcer haemorrhage, or ulcer complications. The risk of bleeding is highest with current use, lower the recent use and least with past use. The risk is higher when two or more NSAIDs are used. It is also dose-related. It is higher in the first month of use, but continues at a constant rate therafter. NSAIDs can best be considered as a class of necessary, but dangerous drugs.[5]

Choosing a Safer NSAID

There is interest in whether it is possible to select a safer class of NSAID, a safer individual drug, dose, route of administration, or whether risk can be reduced by cotherapy with an anti-secretory drug or by replacement of mucosal prostaglandins. There is no evidence that suggest that any one NSAID class is safer than another. The route of administration has not been shown to be important as the frequency of ulcers is similar with oral, parenteral, or rectal NSAID administration[4,9,12]. Prodrugs appear no better than conventional NSAIDs; even administration as enteric coated microbeds does not reduce the frequency of ulcers. The prevailing opinion is that ulcers and ulcer complications are related to systemic effects of NSAIDs on prostaglandin synthesis by the cyclooxygenase pathway. It has been known for some time that the acute mucosal damage (or lack of it) seen in short term

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endoscopic studies did not provide valid predictive information that could be used to rank NSAIDs in relation to safety and that, in general, all NSAIDs appear similar in relation to gastrointestinal complications.

Untoward events are dose-related and relate best to the degree of anti-inflammatory activity. The dose-response curves for anti-inflammatory activity and for analgesia differ. For example, maximum analgesia is obtained with 650 mg of aspirin or acetaminophen which is in turn approximately equal to 200mg of ibuprofen. 400mg of ibuprofen is a more effective analgesic than either aspirin or acetaminophen (Figure 1). Neither 650mg of aspirin, nor 200mg of ibuprofen have significant anti-inflammatory activity and thus these drugs can be given in doses that are primarily analgesic. Nevertheless, no conventionally administered dose of aspirin used for prevention of cardiovascular indications (i.e. 50mg or more per day) appears to be without risk[3]. A small study has shown than 30 mg of aspirin appears not to reduce gastric mucosal prostaglandins[13]. The effect of small doses of aspirin on platelet function is cumulative and two excellent studies have demonstrated that 30 mg of aspirin is equivalent to higher doses in prevention of thrombotic cardiovascular complications. In contrast, piroxicam has analgesic activity only at doses that are markedly anti-inflammatory (Figure 2). Several drugs are available at doses that are primarily analgesic and they appear safest. In contrast, when those same drugs are given at anti-inflammatory doses they appear similar to the other antiinflammatory drugs in terms of complications (Figure 2).

Cyclooxygenase I (Cox I) or Cyclooxygenase II (Cox II) Inhibition?

It is now recognized that there are at least two isoforms of cyclooxygenase (prostaglandin endoperoxide H synthase), often abbreviated as COX I and COX II. COX I is a constitute enzyme that is thought to be important in maintaining mucosal integrity[14]. COX II is inducible and related to inflammation. One hypothesis is that selective inhibition of the COX II enzyme would provide the anti-inflammatory and analgesic activity of nonsteroidal anti-inflammatory drugs without the side-effect associated with NSAID use. There are no selective COX II inhibitors available in the market in the United States; several are in trial. Early experiments suggested that nabumetone had enhanced COX II selectivity compared to other NSAIDs, but more recent studies have not confirmed that hypothesis (Figure 3). it is important to remember that the hypothesis that a selective COX II inhibitor would have efficacy with enhanced safety remains to be proven.

One study which suggested that nabumetone may be safer than other NSAIDs is extremely difficult to interpret because of the study design[15]. Approximately, 50 osteoarthritis patients per group were randomised to receive anti-inflammatory dose of ibuprofen (2400 mg) compared to a largely analgesic dose of nabumetone (1000mg). Patients in the third arm receiving ibuprofen plus misoprostol. The study design differed from prior studies in which endoscopies were performed after the patients had received these drugs for one or more months, to eliminate any confusion arising from the early superficial and meaningless damage. This study included two endoscopies during the early acute phase and most of the patients that were dropped for endoscopic findings were dropped during this interval. Comparison with other studies would limit the comparison with at least the second half of the chronic injury phase of the study and that is the frequency of ulcers with nabumetone was 2% (95% CI=0.4% to 9%) compared to 3% with ibuprofen (95% CI=0.4 to 13% (Figure 4). Thus, comparison of low dose nabumetone with high dose ibuprofen using the paradigm used in previous studies, does not suggest that it is safer than other rprimarily analgesid NSAIDs. In clinical practice, the usual dose of nabumetone is between 1.5 and 2g per day which is higher than the dose studied. Therefore, at present there are no real data to suffice that nabumetone is safer than other NSAIDs with similar ratios of analgesic to anti-inflammatory activity. If the same protocol had been used to evaluate sulindac, one would have anticipated that sulindac, another pro-drug that looks like placebo in acute studies and nabumetone would have looked the same.

It is of interest that whenever comparative studies are done, iburprofen almost invariably appears to be one of the safest NSAIDs. A recent study has shed light on why this occurs and points out one of the fallacies of doing comparative studies without knowing why a particular drug was chosen. For example, a rheumatologist is likely to use ibuprofen in patients with mild disease requiring intermittent therapy, but is much more likely to use a drug with high anti-inflammatory activity such as piroxicam for a patient with a serious inflammatory condition. When patients taking ibuprofen were investigated they were found to be younger, taking fewer other medications, have a lower frequency of arthritis, fewer medical visits, and a more occasional pattern of use than those taking the more traditional anti-inflammatory drugs[16]. These data further confirm the hypothesis that increased anti-inflammatory activity equals increased complications. It also emphasizes that we must attempt to use NSAIDs more rationally.

Two studies have provided important lessons about relative safety of NSAIDs. In 1987, Frank Lanza reported the adverse effects of ketorolac (Toradol$^{(R)}$) on the gastric mucosa[17] Volunteers received either 10,30 or 90 mg of ketorolac parenterally four times a day. The study was stopped when four of five (80%) of the volunteers receiving the high dose of ketorolac developed large antral ulcers at the angulus incisura. The study turned out to be a harbinger of subsequent events. Recently, there has been a revision of the package insert for ketorolac, pointing out the high risk for acute upper gastro intestinal bleeding in patients aged 65 or older receiving parenteral ketorolac for up to 5 days. Recently, another study evaluated flurbiprofen (Ansaid$^{(R)}$) in 40 volunteers[18]. They received flurbiprofen either b.i.d. or q.i.d. for 7 days and 31.5% of those receiving 5.9 mg/kg or moreof the drug developed large gastric ulcers, suggesting that this drug developed large gastric ulcers, suggesting that this drug is also be associated with an increased risk. This is also the first clear demonstration of a dose response (mg/kg) in relation to ulcers. This drug will clearly bear watching.

Why do the elderly appear to be at increased risk for NSAIDS complications?

The elderly typically appear to be disproportionally represented in relation to NSAID associated ulcer complications. This apparent increased risk can possibly be explained by the known increase in baseline risk of peptic ulcer bleeding that occurs with age. If the 3 to 5 fold increased risk with NSAIDs is independent of age, the increased risk in the elderly is simply a reflection of the increased baseline risk (i.e. 3 to 5 times a large number). In addition, chronic NSAID use is largely concentrated in the elderly and endogenous prostaglandin levels may decrease with age.

Co-Therapy to prevent NSAID Ulcer complications

A number of studies have been published evaluating various drugs for their ability to prevent ulcers in NSAID users. Overall, acid suppression and topical therapies have been disappointing. A recent study reported that high dose famotidine was successful in preventing ulcers in NSAID users but the data do not substantiate the claim[19]. The comparator was placebo and 8% of those receiving higher dosages of famotidine developed gastric ulcers which is in the same range as ulcer formation with other H_2-RA studies and markedly higher than that seen with misoprostol. Of interest, the investigators collected data regarding H. pylori status but did not report it. The conclusions ae probably best described as "smoke and mirrors".

Replacement of the mucosal prostaglandins with the synthetic prostaglandin, misoprostol, has repeatedly been shown to be effective in reducing the frequency of both gastric andf duodenal ulcers NSAID users[8,10,20,21]. Sucralfate appears ineffective while the H_2-receptor antagonists reduce the frequency of duodenal ulcers but not gastric ulcers[5,20,22,25] The fact that duodenal ulcers in NSAID users appear more amenable to prevention with acid suppression therapy suggests that duodenal complications in NSAID users are often the result of incidental H.pylori-associated ulcers, possibly exacerbated by the NSAID use. There are little published data concerning proton pump inhibitors but our experience has been that they act more like H_2-receptor antagonists than misoprostol. It has been suggested that high dose omeprazole (40 mg) provides similar prevention as does low dose misoprostol (100ug t.i.d.) but the data have yet to be published. New formulations of misoprostol in a polymer that is only released in the stomach and thus provides gastric protection without systemic effects are in trial but data regarding efficacy are not yet available.

The fact that NSAID related ulcers have not been separated from H.pylori ulcers (or possibly H. pylori ulcers exacerbated by NSAIDs) makes it difficult to generalise or to interpret ulcer healing or prevention studies. New studies that both define ulcer, stratify for ulcer size, and separate ulcers into different possible etiologies are needed before we can make additional progress. At present, misoprostol appears the best choice for prevention of NSAID ulcers. Nevertheless, some patients cannot take it because of side effects such as diarrhoea and abdominal cramps. Misoprostol, like many other drugs, used in the treatment of rheumatoid, arthritis, is contraindicated in women of childbearing age when pregnancy is contemplated.

The recently published misoprostol ulcer complication study provided the first strong indication that co-therapy with misoprostol would not only reduce the frequency of ulcers but would translate into a decrease in ulcer complications. It was confirmed by the MUCOSA trial and suggests that the endpoint of reduction in ulcers in NSAID users can be used as a surrogate for a reduction in risk. Recent studies with H_2-antagonists and antacids have found reduction in risk of patients receiving chronic NSAID therapy which further supports the conclusion of the various misoprostol trials. I recommend that when misoprostol is prescribed it be given as 200ug b.i.d. with meals. This dose is both convenient and well tolerated. Nevertheless, it may be slightly less effective than either 200ug t.i.d., or q.i.d.

Summary

We need to rethink past conclusions about NSAIDs and gastroduodenal complications and also re-do many of the experiments taking into account the H.pylori status of the patient (infected, uninfected, cured). It is predicted that the epidemic of NSAID complications will only get worse. Patients who require NSAIDs and have a history of ulcer should be tested for H.pylori, and if present, it should be cured. Misoprostol should be used more often. If the patient can not take misoprostol, one should consider a proton pump inhibitor. H_2-RAs, including famotidine, provide only a false sense of security and should be avoided as prophylaxis. Only the future will tell whether selective COX II inhibitors of NO-NASIDs that incorporate a nitroxbuty I moiety will actually provide the same benefit at lower risk. Unitl such data become available, we must rely on more rational use of NSAIDs and misoprostol to keep the number of complications at a minimum.

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ORIGINAL ARTICLES

An Outbreak of Dissociative Trance Disorder In a School

Abdul Wahid Khan MD; Tariq Muzzaffar MBBS; Hamidullah Shah MD.

***Abstract:** An outbreak of collective psychopathology took place in a Girls School in Kashmir valley in June 1996. The authors describe the presentation of the same and the features that qualified for it being labelled as an outbreak of Dissociative Trance Disorder. The outbreak was apparently triggered off by a rumour circulating against a backdrop of uninterrupted violence in the valley for the past seven years. The possible etiopathogenesis of the outbreak is also discussed.*

***Key Words:**- Dissociation, Epidemic, Violence.*

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Introduction

Dissociative Trance Disorder is an example of the diagnostic sub-category 'Dissociative Disorders Not Otherwise Specified (NOS)'. belonging to the diagnostic category of Dissociative Disorders, as specified by DSM-IV! A set of research criteria for diagnosing Dissociative Disorder were proposed by DSM-IV.

Epidemics of this nature, when reported in the past, were loosely included under the rubric 'Epidemic Hysteria' as by Francois Sirois[2]. He compiled a set of 78 distinct outbreaks of the phenomenon in the world literature of the previous hundred years (1872-1972). Chodoff[3] termed hysteria 'a fossil encrusted with and obscured by successive layers of meaning,' yet one worth preserving DSM-III[4] dropped the term and split up the fossil into several diagnostic categories. Keeping this in mind, only a minority of the outbreaks compiled by Sirois would qualify for the diagnosis of Dissociative Disorder. The Majority would qualify for the diagnosis of Conversion Disorder as per DSM-IV. In spite of this heterogeneous assortment, these outbreaks shared some important epidemiological characteristics to establish the identity of the phenomenon.[2]

The term 'Epidemic', the descriptive format and the ensuing analysis is derived from the infectious disease model.

The Outbreak And First Case

The school authorities reported to the authors that the first case was a 16 year old girl of Class IX. The girl lost consciousness without any apparent reason, exhibited jerking movements of her limbs, and in an altered state of consciousness attempted to strangulate herself. When these attempts were resisted by the teachers, she pulled at her hair and muttered softly in an altered voice. Throughout the episode her eyeballs showed jerky vertical movements and she was inaccessible for any communication. The episode lasted between five and ten minutes. After regaining normal consciousness, when questioned, she reported that her actions during the episode were not in her control.

There was no history of frothing of mouth, turning of head to one side, urinary incontinence, post-episodal headache or muscle soreness. There was no history of an aura preceding the episode, head trauma or any such previous episode.

Within four days, a total of 20 girls, all belonging to Class IX, exhibited an identical behaviour pattern. These episodes involved groups 2 to 5 girls at a time, and sometimes several such episodes took place in a single day. No other Classes, either junior or the senior class X was affected. The outbreak lasted for two months.

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Measures Taken by School Authorities

The school authorities consulted the local medical practitioners who were of no help. By the time the higher educational authorities could take any step, the outbreak subsided on its own accord. It must be mentioned that the girls' parents consulted the traditional spiritual healers on whom they placed a lot of faith.

Visit of Team from Department of Psychiatry

Three months later, the first case of the outbreak presented to the Psychiatric Out Patient Department of Govt. Hospital for Psychiatric Diseases Srinagar, which is affiliated to the Govt. Medical College, Srinagar. The girl, who had lost her brother in a militancy related incident, was diagnosed as a case of Minor Depressive Disorder and was given an additional diagnosis of Post Traumatic Stress Disorder (PTSD) as per DSM-IV. In the months preceding the outbreak, she had been maintaining an acceptable level of social and academic functioning while under the care of traditional spiritual healers.

Within one week, a team of three psychiatrists, a clinical psychologist and a physician visited the school in question. Informed consent for the study was obtained from the girls' parents and the school authorities.

A retrospective assessment of events was carried out with the help of history taking, physical examination, psychiatric interviews, mental status examination, personality assessment and IQ testing. Epilepsy, food poisoning, CNS infections and substance induced dissociative phenomena were ruled out as a cause. The clinical psychologist's assessment using Eysenck's Personality Inventory, revealed scores high on neuroticism an average IQ. Using Research Criteria for Dissociative Trance Disorder proposed by DSM-IV the diagnosis arrived at retrospectively by consensus is Dissociative Trance Disorder.

Discussion

There have been similar outbreaks of collective psychopathology in Kashmir in the past but the present one is probably the first one to be studied systematically by psychiatrists. Traditional spiritual healers command a great respect among the rural populace in Kashmir and it is a usual practice to consult them either exclusively or in addition to Western allopathic practitioners. As a result, it was not surprising that the outbreak came to the notice of the Department of Psychiatry (the solitary one existing in the valley) rather late.

The circumstances prevailing at the time of the outbreak deserve careful attention. These were unequivocally stressful by any standards. Against a backdrop of unprecedented and unmitigated militancy related violence in the valley, a rumour was circulating in the particular village that the Girls School building would be taken over by the security forces. This led to a wave of panic in the villagers in general and the students in particular.

Of the 78 outbreaks reviewed by Sirois[2],

(i) most of the episodes occured in schools (34), towns and villages (17) and factories(8).

(ii) women were 'almost always exclusively involved', especially in the rural areas.

(iii) most of the subjects were below 20 years of age.

(iv) the number of subjects per outbreak ranged from a few to 200, but most involved a group of less than 30.

(v) the duration of the outbreaks varied from one day to six months but usually ranged between ten and twenty days.

(vi) a triggering event was identified in 39 cases.

(vii) an index case presented in 36 cases.

(viii) in numerous outbreaks, there was an over-representation of lower socio-economic classes.

(ix) frequent associations included a 'state of cultural or ideological transition, periods of uncertainty and social stress like wars, endemic diseases or technological changes'.

(x) the course of most outbreaks was benign and self-limited.

(xi) the disbanding of the group and the isolation of the members was the most effective way to abort an outbreak.

(xii) coercive measures 'like public confrontation' had no benefit and in fact aggravated the situation.

(xiii) 'in outbreaks occuring in larger communities, adequate information to dissipate any panic and mobilize congnitive resources was essential'.

(xiv) the incidence by hysterical epidemic outbreaks was reported to be uncertain. A pilot study conducted by Sirois in the schools of Quebec province in 1973 estimated the attack rate to be about 1 per 900-1000 schools settings per year[2]

Teoh found it endemic in some parts of Malaysia and the same may apply to Africa.[2]

Group Dynamics

In an excellent review on the causatie factors, Sirois[2] attempted to answer the question: Why is the behaviour exhibited by the index case imitated and propagated among the group members instead of being labelled deviant at the onset itself?

It is postulated that a real or imagined threat to a group leads to tension within the group which is released through maladaptive behaviour. The tension can be due to authority-submission conflicts, working conditions or intra-group tension. A situation in which it is impossible to escape can lead to an avoidance-avoidance conflict leading to 'a quasi-ritual solution to collective anxiety'[2]. This view has also been supported by Putman.[5] The abnormal response could be a result of ambivalence, helplessness—actual or learned, failure to mobilize congnitive resources and lack of openness in acknowledging and dealing with the conflict.[2]

The two models suggested for explaining this phenomenon are derived from neurophysiology.

The '*convergence theory*' states that an external threat to a group whose members have common conflict activates the group into an unstable state. This happens frequently in adolescents with confusion about their personal and sexual identity and is amplified by a high degree of suggestibility—a histrionic trait. The high neuroticism scores found among the subjects would support this view.

The concept of '*final common pathway*' which is similar to the 'equifinality concept of systems theory' states that an index case activates disparate conflicts in other group members which are expressed in the 'final common pathway' of identical symptomatology.

Isolation and cohesion of the group prevent verification of the perceived external threats.

The behaviour expressed by the index case, instead of being labelled deviant by other group members, may be felt to be the only solution, however grotesque it may be. It is known that dissociation as a coping mechanism may itself become maladaptive.[6] Once established, the behaviour spreads out into the group through inter-personal networks.

The phenomenon has clinical implications for community psychiatry —a neglected field in this part of the world. School and other educational authorities must start work on primary preventive strategies, planning for crisis management in these tubulent times and maintining quick channels of communication. It also underscores the necessity of conducting community based surveys of prevalence of mental health disorders in the valley, the means for which are sadly lacking in an underfunded and understaffed sector.

Conflict of Interest: None.

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Some Observation on Low-Back Pain in Saudi Patients

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Abstract: *Low back pain (LBP) may cause functional impairment leading to loss of productivity and increased hospital costs in the form of specialised diagnostic procedures and appropriate treatment. 3500 patients (30% of the total) were seen with low back pain in the out-patient department of Al-Zulfy General Hospital between 1983 and 1987. Out of these, a group of 671 patients (19%) with LBP of more than one week duration were selected for this study. Age ranged between 18-75 years (mean 33 years) and sex distribution revealed male preponderance (61.4%). Degenerative spinal disease was found to be more prevalent (60%) followed by work strain (12%), fever (12%), urinary tract infection (8%), spondylolisthesis (3.5%) and spinal infections (2%). The incidence of lumbar disc prolapse was found to be low (3%) as against the high incidence of 80-98% reported in the West. Thorough clinical assessment lead to the appropriate management of the patients and conservative treatment proved to be very effective. This study has highlighted the need for ongoing research to identify other risk factors and tasks in Saudi Arabia that may be causally related to low back pain. It is hoped that the descriptive data of this study will be very useful for health care planners in this country; and the preventive measures tentatively suggested may trigger the development of proper programs for dealing with this problem which has enormous socioeconomic impact.*

Key words: *Low-back pain, Incidence, Epidemiology, Management, Saudi Arabia*

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Introduction

Low-Back pain (LBP) is a benign and a self-limiting symptom. Each year millions of working days are lost by people suffering from LBP and billions of dollars are spent on treatment of this symptom. Saudi Arabia is no exception to this. Problem appears greatest in the Western civilization: the rest of mankind seem to cope with back pain despite an almost total lack of social society, technology-orientated medicine and back surgery.

The annual incidence of LBP has been reported to be 5% and the lifetime prevalence 60%-90%.[1] According to Nachemson (1992) within six weeks 90% of patients with idiopathic LBP resume their work, but recurrence rate ranges from 50%-60% which declines gradually after three of five years.[2] Radiculopathy is present in 1% of patients with acute LBP. Recovery occurs within 4-6 weeks in 50% of cases. Surgical intervention is needed only in 5% - 10% of patients with unrelieved Sciatica.[1] The recovery rate for Sciatica is slower than for patients with idiopathic LBP.[2] Unfortunately, in 50% of patients with LBP exact cause is not known. Even after thorough laboratory and radiological evaluations, only 10%-20% are given a precise pathoanatomic diagnosis.[1,3] However, the concept of basic neurophysiologic pain mechanisms is gradually becoming better understood after recent discovery of the free naked nerve endings in the outer part of the annulus fibrosus, in the dorsal ligament, and in the facet joint capsules.[2] Self care is enhanced by education in exercise and correct use of the back in routine life[4] since prognosis for LBP is favourable, so proper assessment, good conservative care, aggressive rehabilitation and timely surgical intervention in the selected cases determine the outcome in most cases, if not all.[1]

The purpose of this study was to find out the incidence and aetiological factors of LBP in Saudi patients which may initiate any discussion for the prevention and related medical care and suggest an agenda for further research in this field.

Material and Method

This study was carried out on 671 Saudi patients

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with low back pain of more than one week duration who attended the Orthopaedic clinic of Al-Zulfy General Hospital between 1983 and 1987. Relevant history was collected and thorough clinical examination conducted on all patients. This included record of patient's, age, sex, occupation, past history of any illness, personal history, pain radiation, and type of previous treatment, if received. Haemogram and urine analysis were done routinely. In some patients, in addition, appropriate biochemical (serum creatinine, urea, calcium, phosphorus, alkaline phosphatase and liver function tests) and serological tests (Rheumatoid factor and Brucella titre) and plain anteroposterior and lateral radiographs of lumbar spine in 473 patients were done. Fifty eight patients were referred to nearby hospitals for computed tomography (CT scan) to establish a definite diagnosis. Patients with severe LBP, who were brought to clinic on trolleys or wheelchairs were admitted to the hospital for treatment (bed rest and analgesics), all other patients were treated in Outpatient department on the same lines of management for two weeks. For those who did not respond to drugs, short wave diathermy (usually ten sittings) was added followed by exercises. In some non cooperative admitted patients, pelvic traction was applied to confine them to bed.

Al-Zulfy Hospital is one of the old general hospital in the Kingdom of Saudi Arabia with a bed capacity of 200 beds. The hospital has Outpatient department, Laboratory, Blood bank and radiology facilities for Medical, Surgical, Gynaecological and Obstetrics, Paediatrics and Dental disciplines.

Results

3,500 patients (30% of the total), all Saudi nationals, with LBP attended the Orthopaedic clinic during the four year study period. Of these, 671 patients (19%) had LBP of more than one week duration. Age of patients ranged from 18-75 years with a mean age 33 years. Males were 412 (61.4%) and females 259 (38.5%). 305 male patients were sedentary workers (involved in some business or desk work), 89 were shopkeepers (involved in repetitive lifting and carrying), and 18 patients were working in some factories (involved in twisting, pulling, pushing, etc). Most of the female patients were housewives: a few were school teachers. 362 patients were smokers. Type of pain was mild in 197 cases (29.3%), moderate in 311 (46.3%) patients, and severe in 163 (24.3%) patients. Clinical profile of patients is detailed in Table I. Eight out of 19 patients with lumbar disc prolapse between L4 - L5 and L5-S1 had radiculopathy. Neurodeficit found in 51 patients was in the form of calf muscle wasting. Motor weakness (usually Extensor hallucis longus), subjective hypoasthesia in the leg and the foot, and absent ankle jerk. More than one finding was observed in most of these patients. No patient had neurogenic claudication. The patients received same treatment as practised anywhere else i.e., short period of bed rest (4-5 days), in addition to analgesics followed by exercise programs. After this, those patients gradually returned to their routine work. Surgery was advised in 11 cases with unrelenting radicular pain and objective radiculopathy.

Discussion

Low-Back pain is the most common musculoskeletal symptom which may cause significant disability and it has tremendous socioeconomic importance. The occurence of LBP is so common in everyone's life that in fatigue or even in common illnesses like flu, it may be one of the main symptoms. In present study 12% of patients with fever and 8% with urinary tract infection presented with LBP.

It has been predicted that about 70-80% of the general population will suffer from LBP at some stage of their lives.[3,5,6] The incidence of LBP in 30% of patients attending our clinic does not support this statement. The lifetime prevalence of LBP lasting at least 2 weeks has been reported to be 13.8%.[7] The incidence of LBP of more than one week duration in our series was found to be 19%.

First episode of LBP occurs usually between the ages of 20 and 40 years.[6] Prevalence rises after 25 years and reaches a peak in the old-age range of 55-64 years, but few cases begin before the age of 20[7]. Men and women are equally affected.[8] Frymoyer et al. (1980) reported age range of 18-55 years with mean age of 34.6 years in males and 35 years in females in their study.[9] As regards age our results nearly concur with those of Frymoyer (1980) except that age range in our series was on the higher side (75 years). The lower incidence of females (38.5%) in present series was probably related to the social habit in Saudi Arabia where females are more protected. The incidence of LBP was higher among subjects with low educational level and declined steadily with increasing educational status. Most of patients in this series had low educational level thus, supporting this observation. LBP has been significantly related to smoking, strenous occupations, physiological factors (menstruation, pregnancy and childbirth), damp and cold environment and psychological factors like anxiety and depression[1,2,3,9,10]. The current study supports these findings of previous studies as 54% of patients in this series were smokers and many patients related their illness to drop in weather temperature or some domestic events like serious illness or death of a family member or a relative etc. Hypotonic abdominal musculature produce lumber hyperlordosis which is an important cause of LBP in females;[11] and LBP is more common in multiparous women.[9] Our observations are in accordance with these facts as majority of our patients were multiparous and were over worked with household work and child care. Previous epidemiological surveys have identified several other important factors in the pathogenesis of LBP and radiculopathy.[1,2,3.] A notable observation in this study was the highest incidence of degenerative spinal disease (60%) and low incidence of lumber disc prolapse in 3% of patients (Table I). It is our impression that the former could probably be due to sedentary life style, obesity and lack of exercise while the latter due to flattening of the lumbar spine during sitting and squatting postures which form essential part of social. and cultural habits of the Saudians. Our presumption is based on the reported evidence that disc degeneration is rare in individuals who habitually sit or squate in postures that flatten the lumbar spine because flexed postures reduce the stresses on the posterior elements (apophyseal joints and posterior half of annulus fibrosus) and gives the spine a high compressive strength.[12] Moreover, 98% of disc herniations occur at L4-L5 or L5-S1 levels, often with radiculopathy and most patients are between 20-50 years of age.[1] The site of maximum load-bearing stress is L4-L5 and is quite often the first disc involved in acute disc herniation.[13] We found 42% incidence of radiculopathy in 19 cases of lumbar disc herniations and age ranged from 25 to 47 years.

Degenerative spinal stenosis includes degenerative spondylolisthesis and degenerative lumbar spinal stenosis, affecting either the central canal or lateral recesses.[1] None of our 400 patients in degenerative spinal disease group (Table 1) presented with neurogenic claudication. Presumably they had a wider spinal canal, although we did not measure the canal in these cases as it would have needed another study of greater magnitude. Plain radiography has a limited role in finding a definite cause for LBP[1,2,14], but isotope bone scanning, computed tomography and magnetic resonance imaging have a very valuable role in diagnosing different pathoanatomic lesions causing this symptom. Since facilities for such investigations are available only at some specialist centres in the Kingdom, we feel that their misuse can be minimized by completing the necessary preliminary investigations at peripheral centres, and if possible, prior expert opinions is sought before referring patients to these centres or exposing patients to undue radiations.

Table-1
Clinical Presentation of Cases

Diagnosis	Numbr of patients	Percentage of the total
Fever	78	11.5
Urinary tract infection	53	8
Work strain	82	12
Lumbar disc prolapse	19	3
Osteoarthritis -181-- Osteoporosis - 156-- Osteomalacia - 63--	400	60
Spondylolisthesis	24	3.5
Tuberculosis, Brucellosis	14	2
Secondaries	1	-
Total	**671**	**100**

The relief of pain and improvement in function following surgical treatment of lumbar disc herniation and radiculopathy are short-term benefits. Nevertheless, 2.5% of patients with sciatica (cauda equina syndrome) and 5% of patient with significant neurodeficit (such as foot drop) are often best treated surgically.[15,16] In our series surgery was advised in 11 patients, but these individuals were unwilling to have an operation and were referred to the Neurosurgical Department at Riyadh Central Hospital.

Conclusion

We found that the incidence of low back pain lasting more than one week in Saudi patients, presenting to the clinic, is 19% which is much less than that reported in the Western populations. Degenerative spinal disease (60%) was the most frequent risk factor with which it was associated; possibly as a consequence of sedentary life style of these patients. The finding of low incidence of lumbar disc herniation (3%) is reverse of that seen in the West. So more studies are needed to further confirm these observations and to find out the prevalance and other risk factors responsible for this spinal disorder in Saudi Arabia. For prevention of low back pain, health care awareness should be increased in the general population and the education system must give it due care.

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Early Breast Cancer - Lumpectomy Followed by Radical Radiotherapy

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Abstract: *The aim of research in early breast cancer during the past few decades has not been only to increase the long term survival but to improve the quality of life as well, by obtaining better cosmetic results and acceptable morbidity. Conservative surgery in the form of lumpectomy followed by radical radiotherapy in early breast cancer has been an excellent alternative to more radical procedures like mastectomy and it has yielded excellent cosmesis, in addition to comparable results as far as local tumor control and overall survival are concerned.*

Key words *: Early breast cancer, Conservative management, Local control, Cosmetic results.*

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Introduction

Conservative surgery in the form of lumpectomy, followed by radical radiotherapy for early breast cancer is being increasingly used as an alternative to more radical treatment approach in the form of mastectomy. In order to assess the cosmetic results of treatment, the results in 88 patients with early breast cancer treated by lumpectomy followed by radical radiotherapy were studied prospectively. The parameters studied were breast edema, retraction, telangectasia, arm edema, overall cosmetic appearances and locoregional control. The cosmetic results tend to stabilize. Breast and arm edema were early noted and cosmetic results were excellent or good in over 85% of patients. In general, it appears that conservative treatment provides highly satisfactory cosmetic results for patients with early breast cancer.

The modem management of early breast cancer aims at preserving the aesthetic aspect of breast without compromising the chances of local control. In recent years there has been an increasing interest in the treatment of breast cancer by lumpectomy and radiotherapy. Both un-controlled (6) and controlled(27) series have shown that this method of treatment produces rates of local control and survival comparable to those achieved by conventional mastectomy.

The management of early breast cancer today focuses on local therapy with the new trends in surgical techniques and development of megavoltage irradiation, which has fulfilled the aim to provide satisfactory cosmetic results with minimal/no radiation sequelae. This procedure alone - lumpectomy followed by radical radiotherapy - is justified as the primary treatment for early breast cancer. The survival rate is comparable to that obtained by standard surgical procedures, the post-radiotherapy sequelae which are acceptable, provide satisfactory cosmetic results and a decrease in overall morbidity.

Lumpectomy has been criticized because of the high incidence of multi-focal disease within the breast of the order of 30%(12). Because of this multicentricity it was argued that local control may not be achieved by any procedure less than total mastectomy(25). Since the biological behaviour of breast cancer within the breast itself is unpredictable, the purpose of radiotherapy following lumpectomy is to sterilize the microscopic disease in order to reduce the local recurrence rate. The dose of radiation used is adequate to sterilize the subclinical disease in the breast and lymph nodes and has given good cosmetic results with no undue sequelae.

The most distressing complication of a radical surgery is arm lymphoedema. During the era of Halsted radical mastectomy, the incidence of *lymphedema* was reported at 6.7% to 62.5%(27), while lymphatic obstruction consequent to axillary clearance is an obvious cause of *lymphedema*, Britton and Nelson(4)

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thought that super-added infection was important while Hughes and Patel$^{(15)}$ blamed obstruction of the axillary vein. With the adaptation of more conservative procedures in the management of breast cancer the risk of arm lymphedema appears to have decreased. Thus the reported incidence includes 15.4% after modified radical mastectomy$^{(13)}$, 2.1% and 3.1% after wide local excision and total axillary clearance$^{(13)}$ and 2.3% after local excision plus radiotherapy$^{(27)}$.

Evaluation of arm *lymphedema* is part of a battery of objective cosmetic analysis we have performed on patients treated conservatively with breast conserving treatment for breast cancer. Because the major advantage of radiotherapy is breast preservation, attention to factors that maximize the cosmetic results is becoming more important.

The treatment of early breast cancer remains controversial despite multiple clinical trials and much has been written by opponents and proponents of conservative surgery followed by radical radiation as an alternative for the more clinically accepted radical or modified radical mastectomy. One of the aims of this study is to summarize our experience with early breast cancer with respect to cosmesis in particular, using these conservative therapeutic modalities and to examine how these results change with time and which factors may have an influence.

Material and Methods

Between 1988 and 1993 we enrolled 4190 cancer cases in our central cancer registry out of which 7.2% constituted breast cancer. 88 patients were diagnosed as having early breast cancer (Stage I & II) and these patients were considered in this study. Criteria included:

i. Awareness
ii. Tumor - peripheral
iii. Lesion size - only T1 and T2 lesions
iv. Tumor - small in relation to breast size
v. Single tumor - pre-operative mammogram
vi. Tumor margins - well defined.

All patients had a histologically proven diagnosis of breast cancer and were staged according to TNM classification. 61 patients had T_1 lesion, while as 25 patients had T_2 lesion and in two cases the T staging was ambiguous.

The treatment protocol consisted of surgery in the form of lumpectomy for the primary lesion. The lumpectomy incision was made directly over the mass. The tumor and 2-3 cms of grossly normal tissue were excised and, care was taken to ensure total excision of cancerous areas. Of the 18 patients with axillary involvement,9 patients had axillary dissection and 9 patients had axillary sampling. In the axillary dissection group only 4 patients had radiotherapy to axilla and in the axillary sampling group, all patients had post-operative radiotherapy to the axilla.

Pre-menopausal women with positive axilla received adjuvant chemotherapy in the form of "CMF" for a total of six such cycles. The CMF regimen consisted of Inj.Cyclophosphamide 600mg/m^2 I.V, Inj. 5-Fluorouracil 750mg/m^2 I.V. and Inj. Methotrexate 50mg/m^2 I.V. given on day-I and 8 with a gap of 21 days from the end of one course to the begining of the next, checking the haematological parameters and kidney status. This was continued to a total of 6 cycles. Post-menopausal women with positive axilla were subjected to hormones (anti-estrogen - tamoxifen citrate 20mg daily).

All patients were screened to rule out occult osseous/ visceral metastasis in the form of:-

☐ Complete liver function tests
☐ liver scan
☐ skeletal survey
☐ bone scan (where indicated)

The radiotherapy treatment was delivered by Megavoltage radiation.

1. Breast was treated by two tangential fields, after proper planning on a simulator to avoid lung tissue from being irradiated unnecessarily. A median dose of 40 Gy in 15 fractions over 21 days was delivered with a Cobalt-60 unit. Thereafter, all patients received boost to local area with electron beam therapy or Cobalt-60 beam to a dose of 15 Gy in 6 fractions over 8 days.
2. Ipsilateral supraclavicular fossa and axilla were treated in all the patients by Co60 beam to a dose of 40 Gy in 15 fractions, over 21 days.
3. Internal mammary nodes were treated in patients who had a centrally placed or inner quadrant breast tumor. The dose delivered was 40 GY in 15 fractions over 21 days.

After completion of treatment, all patients were followed up at regular intervals in a joint breast clinic. (Table - I)

Table-1: Follow-up tests during specific intervals

Investigations	Before treatment	6 wks. after treatment	For 2 years at 3mo	6mo	12mo	For 3-5 yrs. 6mo	12mo
Mammography							
Healthy breast	x	-	-	-	x	-	x
Treated breast	x	-	x	-	-	x	-
Chest X-ray	x	x	-	x	-	-	x
Bone Scintigraphy	x	x	-	x	-	-	x
Haematology and blood chemistry	x	-	x	-	-	x	-

The breast cosmesis was assessed at each follow-up, and were graded as follows:-

Grade	Objective Assessment	Subjective Assessment
1.	No obvious change in size of breast, texture skin appearance.	No physical discomfort. Full physical activity of arm. Patient feels normal.
2.	Breast deformity but limited to one quadrant, nipple in normal position. Minimal hyperpigmentation or skin atrophy. Palpable change in skin texture.	Minimal discomfort. No arm disability Occasionally aware of a difference compared with other breast.
3.	Moderate breast deformity involving more than one quadrant. Nipple position obviously changed. Moderate skin atrophy. Obvious hyperpigmentation or atrophy or telangectasia.	General discomfort. Minimal limitation of arm movement. Patient aware of difference.
4.	Marked breast distortion. Marked fibrosis, hyperpigmentation, telangectasia, skin atrophy or oedema.	Continual discomfort. Obvious limited arm movement. Patients embarrassed by difference.

The arm circumference was measured at each follow-up. The circumference of each arm was measured 15 cm above the lateral epicondyle with a tape measure with the elbow flexed at 90° and shoulder in the anatomical position. Care was taken to avoid constriction of soft tissue by the tape.

Results

The mean follow-up was 66 months. Majority of patients were in the age group of 40-50 years. Right breast involvement was seen more than the left although with a marginal difference. The upper and outer quadrant was the most common site of primary tumor whereas lower inner quadrant was the least common site of the primary tumor.

Out of the total number of 88 patients studied, 70 patients were subjected to only lumpectomy, 9 patients to lumpectomy with axillary sampling and 9 patients were subjected to axillary dissection. All the 9 patients subjected to axillary sampling had radiotherapy to axilla whereas 4 out of 9 patients who had axillary dissection received radiotherapy to axilla.

The patients were followed up and the loco-regional control, cosmetic results, complications and survival was assessed at regular intervals for a maximum follow-up of 66 months. The cosmetic results were good to excellent in 85% patients. 2% of patients developed breast fibrosis which was not so marked that it could be included in grade IV cosmetic score. None of the patients had grade IV cosmesis. (Table 2).

Table-2: Cosmetic Results

Grade	Objective	Subjective
I	76	72
II	40	32
III	09	02
IV	-	-
No mention	02	01

Only one patient in our series developed frank arm lymphedema and this patient had received radiotherapy to axilla following axillary sampling.

Analysis of the complication and sequelae that were seen in these patients revealed that dry desquamation was the most commonly observed sequela. No major complication except arm lymphedema in one patient and mild breast fibrosis in two patients were seen (Table-3).

A total of 8 patients (9%) developed loco-regional recurrence at five years. Out of them 2 recurred in the axilla and 6 locally. All the 6 patients who recurred at local site had T_2 lesions at presentation and were salvaged with mastectomy. The two patients who recurred in axilla also had T_2 lesions and had no previous surgical interference to axilla but had radiation therapy to axilla (40Gy/15 fractions). This observation of ours is depicted in tables 4 and 5 where we have compared our results with that in the literature.

Table-3: Complications - Conservative Surgery and Radical Radiotherapy

Study	No. of patients treated	Breast fibrosis	Pneumonitis	Arm edema	Rib fracture	Breast edema
Pronitz[23] *et al* (1982)	150	-	2.5	1.5	3.5	-
Calle[7] *et al* (1983)	120	11	5	2.5	8.5	-
Montague[18] *et al* (1979)	263	14* 4**	9	7	1.5	22
Pierquin[22] *et al* (1980)	150	-	2.5	1.5	3.5	-
Harris[16] *et al* (1979)	184	-	3	0.5	5	-
Varonesi[27] *et al* (1981)	352	1.5	-	3	-	-
Ray[24] *et al* (1983)	130	13	-	11	4	35
Present study	88	2	-	1	-	-

* *Severe fibrosis at field function.*

** *Severe fibrosis entire breast.*

At five years, the overall and relapse free survival in this series was 95% and 79% respectively (table-4).

Table-4: Primary Local Excision and Radical Radiotherapy

Author	No. of patients	Clinical stage	Survival (%) 5 yrs	RFS (%)	Loco-regional recurrence rate (%)
Amarlic[2] (1982)	1099	I & II	72	68	10
Montague[11] (1979)	169	I & II	86	86	4
Pierquin[22] (1980)	134	I & II	82	77	7
Prosnitz[23] (1980)	293	I & II	85	74	8
Veronesi[27] (1982)	352	I	89	83	-
Present study (1996)	88	I & II	95	79	9

Two patients were harbouring disease in bones and two patients in chest wall, whereas 3 patients died due to metastatic disease. One patient died of an unrelated cause.

Table-5: Axillary Recurrence after Local Excision plus Radiotherapy

Study	Stage	Prior axillary dissection/ sampling	Axillary dose (Gy/#/days)	Axillary recurrence (%)	Follow-up (yrs)
Montague[18] *et al* (1979)	T1-2, N0-1	45/162	50/25/35 +10Gy boost	1	2-22
Pierquin[22] *et al* (1980)	T1,N0-1 T2,N0-1	0/43 0/91	45/25/35 +24Gy Boost	0 1	≥5
Harris[16] *et al* 1979)	T1-2,N0-1	0/184	46/23/32 ±Boost	2	3-12
Present study	T1-2,N0-1	18/88	40/15/21	2.3	1-5

Discussion

Conservative treatment for early breast cancer is increasingly being performed. Retrospective studies(18) and preliminary data from randomized trials comparing mastectomy and conservative management(27) indicate no significant difference in survival and distant recurrence, but the advantage of a conservative approach is its superior cosmetic results. Some studies, while comparing the results of widespread tumor excision followed by radical radiotherapy, showed a major role of radiotherapy in achieving local control(11-20).

The aims in the management of patients with early breast cancer are two fold. The first aim is directed towards attaining the best cosmesis possible without compromising the patients chance of cure and the psychological morbidity associated with mastectomy is reduced. The conservative therapy has been allocated for improvement of cosmesis rather than to prolong disease free survival. It was hoped at the time of allocating the conservation therapy that cosmetic benefits could be achieved even with treatment failure and survival possibly equivalent to that obtained by more radical procedures. There was, however, the possibility that unremoved axillary nodes might be immunologically advantageous to the host. This concept requires still consideration. Data from the studies conducted so for fail to substantiate this idea.

The cosmetic results reported in many series are satisfactory and comparable with other reports(5,6,24). However, it needs to be noted that with the passage of time the results tend to deteriorate, thus stressing need for prolonged follow up. There are many factors that affect the cosmetic results. The important ones being tumor size, surgical and radiotherapeutic techniques. Not surprisingly, the presence of a post-surgical defect has a significantly adverse effect on both the overall cosmetic results and the degree of asymmetry.

Since the surgery compromised a wide excision of the tumor, a uniform policy was laid down in this series for local surgery, the technique of breast irradiation did not change during this period and radiotherapy protocol was adhered to. similarly all patients received a boost to the tumor bed without any variation in techniques and total dose.

In our study, we noticed a 9% loco-regional recurrence rate. Out of 8 patients who recurred, 6 did so locally whereas 2 patients recurred in axilla. All these patients had T_2 lesions at presentation and the 2 patients who recurred in axilla had no prior axillary surgery but had received external radiotherapy to axilla (40 Gy/3 weeks/15 fractions) (table-6).

Table-6: Status - Loco-Regional Recurrence at 5 years

Study	T1	Breast NED	T2	Breast NED
Pierquin B[21] (1983)	3/99 (3%)	82/83 (99%)	15/235 (6%)	169/177 (95%)
Present study	0/61 (0%)	61/61 (100%)	8/25 (32%)	17/25 (68%)

NED = No evidence of disease

The incidence of local recurrence following lumpectomy seems to depend on the radiation dose delivered. Mustakalio(19) reported 24% local recurrence rate at ten yearsfollowing low dose conventional irradiation. Atkins *et al*(3) using a 6Mv linear accelerator gave the breast 35-38 Gy tumor dose in three weeks and using 300 KV unit gave the apex of the axilla between 25-27Gy tumor dose in three weeks. They reported a 20% local recurrence rate at 5 years. The techniques of exclusive radiotherapy which are used for treatment of breast cancer following lumpectomy are really difficult to assess but are simple if done accurately after proper planning but definitely need a great deal of supervision. The cosmetic results were either excellent or good in over 85% of patients. This justifies the conservative management of breast in the form of lumpectomy followed by radical radiotherapy, especially if tumor is unifocal, equal to or less than T2 lesion and without any interference to the axilla. Whereas the result of local control of early breast cancer with conservative management and significantly good cosmetic results overall may be satisfactory, however, attention to certain factors that maximize the cosmetic results is becoming more important. One major complication is the arm lymphedema. One factor contributing to arm lymphedema is the axillary interference followed by its treatment with radiotherapy. This has commonly been considered a complication of external beam irradiation, however Clarke *et al*(8) reported in their series that this complication arises primarily from axillary staging procedure. Arm lymphedema and breast edema developed in 79% of their patients who underwent axillary node dissection as opposed to 12% of patients who had axillary sampling or no axillary surgery at all. This finding clearly demonstrates the importance of axillary route of breast lymphatic drainage. In the series of Clarke *et al*(8), lymphedema of breast was a frequently observed complication. They identified two groups of patients -those with acute or early onset breast edema and another with late onset. Early breast edema appearing before or during external beam radiotherapy was found to be related to the disruption of lymphatic flow after axillary dissection. Other potential factors such as breast and axillary dose, fractionation schedule, use of bolus, breast size and stage could not be found contributory. Furthermore, they noticed late breast edema occurring 20 months or more post-irradiation, rarely. The three patients received high radiation dose to the axilla, indicating that a state of chronic and late lymphatic insufficiency had been induced. None of these patients showed any improvement, suggesting that this entity may be irreversible.

Analysis of the cosmetic results following lumpectomy and radical radiotherapy has shown that the majority of patients have a satisfactory outcome (7-16). The frequency and severity of arm lymphedema is mainly related to use of an axillary dissection procedure. Arm lymphedema is reported to be rare when axillary dissection was not performed. In our series, only one patient developed arm lymphedema and this patient had been subjected to axillary sampling and external radiation therapy to axilla. In a series of patients, Geoffrey *et al*(13) noticed that no undissected patient had developed arm lymphedema at even 6 months post treatment and only 2% had arm lymphedema at 30 months. In comparison he reported 6% of patients undergoing axillary dissection had arm lymphedema at six months (p=0.3) and 12% at 30 months (p=0.54). Furthermore, he reported that incidence of arm edema was slightly higher at 6 and 30 months in their group having 11 or more nodes removed than those having 1 to 10 nodes removed, but however, this difference did not reach statistical significance. The frequency of breast edema itself, which is of more concern to the patient, is reported to be highest at 6 months and then diminishes with increasing follow-up. Geoffrey *et al*[13] noticed that at 6 months, 75% of his patients not having axillary dissection were free of breast edema compared with 60% of those undergoing dissection (p=0.30). At 30 months the corresponding figure was 87% and 78% while at 48 months the figure was 94% and 83% respectively. When the number of axillary lymph nodes removed at dissection is used as a guide to the extent of surgery, patients having 1 to 10 nodes sampled were noted to have a lower frequency of breast edema at all time points than patients having 11 or more nodes sampled. This difference appeared most striking at 6 months, when only 46% of patients with 11 or more nodes sampled were free of edema compared with 64% of those who had 1 or 10 nodes sampled (p=0.19). However, most of these differences in the incidence of breast edema in dissected and undissected patients is due to minimal change only. This is also supported by the observation of Clarke *et al*[8], who noted that only 2 of 31 patients (6%) without an axillary dissection developed breast edema. When 1 to 6 nodes were removed, 3 of 12 patients (25%) and when more extensive axillary dissection was performed, 26 of 33 patients (79%) developed breast edema. While as undissected patients had a very small incidence of breast edema, this was noted further to be associated with increasing frequency of mild arm- lymphedema. They reported that at six months, 6% of patients had mild arm lymphedema following a limited dissection while as Demoss *et al*[9] noticed arm lymphedema in 17 of 77 patients (22%) following a complete axillary dissection. We did not observe breast edema in any of our patients.

The arm-lymphedema in patients treated for breast cancer has been investigated by many authors and this has been the subject of considerable debate, and mainly attributed to lymphatic obstruction. For patients, treated by breast preservation techniques, full axilla radiotherapy following axillary dissection has been considered significant. Durand *et al*[10], found arm lymphedema in 9% of patients who received 55 Gy to full axilla and regional nodes following arm node dissection, whereas they found arm lymphedema in only 1% of patients with axillary node dissection and without further treatment to axilla. A combination of axillary surgery and radiotherapy have been found associated with significantly increased risk of arm-lymphedema. No doubt, it has been related to the extent of axillary surgery, the dose of axillary radiotherapy and the number of nodes removed. It is also worth remembering that late arm lymphedema may be due to axillary clearance in up to 15% of cases. A review of five major trials of breast conservation reveals an arm-lymphedema rate varying from 2.3% to 2.7% (14,25). The major problem in assessing the impact of breast conservation on the development of early/late arm lymphedema is the lack of a universal definition of the lymphedamatous arm. Definitions that have been employed include difference in arm circumference of >1.5 cm to 5 cm, or difference in arm volume of >20% and >40%. various methods have been used to measure the arm circumference. The traditional way is use of tape measured arm circumference 10 cm below or 15 cm above either the olecranon or lateral epicondyle. We have been using the same method and defined arm lymphedema as a difference of 2 cm or more in arm circumference which is persistent but care needs to be taken to avoid constriction of soft tissue by the tape measure the observer uses. Kissin *et al*[17] tried to examine other factors related to arm lymphedema. In their observation the only factors that were significantly associated with arm lymphedema were surgery to axilla (p=0.03), radiotherapy to axilla (p=<0.001), radiotherapy to the breast (p=<0.001), T stage (p=0.02) and pathological nodal stage (p=<0.001). When the above factors were fitted in a logistic regression model using a step-down procedure, only radiotherapy to axilla (p<0.001), surgery to axilla (p<0.05) and PN stage (p<0.10) were found to be independent risk factors at the 10% significant level.

Considering the dangers of axillary recurrence, it is necessary to identify women with a probability of isolated axillary lymph node relapse and to select these patients for elective lymphatic irradiation. A parallel aim is to adopt a careful watch policy in patients judged to be at low risk of lymphatic relapse and to examine them every three months during the first three year of follow-up . As after axillary dissection,the histologically node negative patients run a very small risk of lymphatic recurrence and hence regional radiotherapy should be withheld.

Many investigators further tried to attempt to determine whether or not the use of a boost to the primary tumor area influenced the cosmetic outcome. The analysis was limited to the fact that majority of patients received a boost. The results however indicate that the use of a boost was associated with increased likelihood of breast retraction and telengectasia. We do not believe this observation should have major impact on clinical practice, for a number of reasons. Since the local control and cosmetic results remain the primary objective of treatment, the cosmetic outcome was highly satisfactory, we continue to advocate the routine use of boost in these patients.

At 5 years, the overall and disease free survival in our patients was 95% and 79% respectively. These findings of ours are comparable to other studies (table-4).

The conservative management has a tremendous psychological impact. Aaronson *et al*(1), reported data on psychological impact in two groups of patients, one with radical mastectomy and the other group with conservative therapy. The results indicated that conservative group reported significantly better body image and greater acceptance of bodily change and less employment disability. Contrary to the expectations the fear of disease recurrence was noted more frequently among radical mastectomy than in conservative management group. This finding is quite important.

Furthermore, the priority in evaluating the efficacy of conservative management of early breast cancer is to integrate quality of life evaluation into the standard battery of end points used in the evaluation of clinical outcome. This requires careful attention to the development of valid, reliable and standardized measures.

This is particularly important if we hope to undertake meaningful analysis of some of the rare events associated with early breast cancer and its treatment.

Conclusion

Conservative management in early breast cancer (lumpectomy followed by radical radiotherapy) results in:

a) Low incidence of local failure.
b) Disease free survival and overall survival comparable to more radical procedures.
c) Good to Excellent cosmetic results.
d) Negligible risk of arm lymphedema.

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Tumors of Jaw in Kashmir Valley: A Clinico-Pathological Profile

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Abstract: *A clinical and pathological review of 93 cases of jaw tumors treated in Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar in 10 years is presented. Carcinomas of various types of jaw including those of maxillary antrum were of the commonest lesions. Out of 14 odontogenic lesions, ameloblastoma was seen in 8 patients, and epithelial jaw cysts in 6 patients. No secondary tumors were detected. Some of the very rare tumors found in this study were those of a rhabdomyosarcoma of maxilla in two patients, schwanoma in one patient and malignant melanoma in one pateint.*

Key Words: *Jaw tumors, Carcinoma, Ameloblastoma, Dentigerous Cyst.*

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Introduction

Tumors of the jaw are common in Africa and most of the literature on these tumors has been published from the same area.[1,2,3] Jaw tumors are not uncommon in the valley of Kashmir. Over a period of 10 years (1984-1993), 93 patients of jaw tumors presented for treatment at the Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar which is the largest referral centre in the valley for managing such patients. The present study was undertaken with a view to study clinical and pathological behaviour of these tumors in the valley.

Material and Methods

The records of patients with jaw tumors admitted from 1984 to 1993 in the Institute formed the source of material in this study. The case files in respect of clinical history, investigation and histopathological report of the specimens and biopsies sent for examination were studied critically and recorded on a proforma. The tumors were grouped accroding to classification suggested by Pindborg and Krammer as adopted by World Health Organization (1971)[4].

Results and Discussion

On analyzing the records, various types of lesions found in our patients are shown in Table I. Various groups and some of the specific tumors are discussed as follows:

Odontogenic Lesions: They are intraosseous lesions arising from the tissues responsible for tooth development.

Ameloblastoma: There were eight patients of ameloblastomas in this series. Youngest patient was a 12 year old male while oldest was a 45 year female. Majority of patients were seen in 2nd and 3rd decade of life with a mean age of 23.9 years at presentation. Male to female ratio was 3:1. Seven patients (84%) had involvement of maxilla. Our results are consistent with those of Dodge[3] who had 24 patients of ameloblastoma in 117 patients of jaw tumors in Uganda Africa, mean age of presentation being 32 years. Male to female ratio was 2:1. Mandible involved in 80% patients and maxilla in 20%. Robinson[5] made a survey of 379 cases of ameloblastoma from literature and found an average age of 30.1 years at presentation. 83.7% were in mandible while 16.3% were in maxilla. Sex distribution was different from our study and showed female involvement in 54% cases which was because sex was not mentioned in 58 patients in the literature he studied. Our study differed from those of Small and Walderon[6] who in a review of 1039 cases

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found mean age at presentation of 38.9 years. Distribution of the lesions was equal between two sexes. Dhaliwal[7] found 32 cases of ameloblastoma in a review of 213 cases of jaw tumors and found 88% lesions involving lower jaw and 12% upper jaw, however, he found equal distribution of lesions between two sexes which is different from our study.

Six patients (75%) presented with painless swelling of jaw . Pain was present in three (38%) patients, the results being consistent with those of Mehlisch.[8]

Radiological examination revealed grossly trabeculated zone of osseous destruction that had the appearance of multilocular cystic cavity in three patients. The bone appeared to be replaced by a number of well defined radiolucent area that gives the lesion a honey-comb or soap bubble configuration in two patients. Two patients showed a well defined area of radiolucency that suggested a single compartment.

Maxillary lesion in one patient showed a monocystic cavity.

Ameloblastic fibroma: This tumor was seen in mandile of a 6 year old male child in the regions of molar area. He presented with painless swelling of the mandible of one year duration. X-ray of the mandible showed a unilocular radiolucent lesion. Average age of detection of these tumors is 15 to 25 years, though cases have been reported in young children.[9,10]

Fibrosarcoma: Four patients with fibrosarcoma seen in the series were of age of 2 years male, 9 years male, 20 years female and a 50 years old female. Two patients had involvement of maxilla and two patients had involvement of mandible. Principal symptom of patients was swelling of the jaw of 6 months to one year duration. Radiographic features included radiolucent shadow of the involved bone and rarification of plate was seen in one patient with maxillary tumor.

Kevin[11] in a study of 49 cases of primary tumors of mandible found four patients of fibrosarcoma. Age ranged from 30 to 50 years. Pain and swelling of jaw were the presenting features.

Anand[1] in his study of tumors of jaw in West Africa found seven patients of fibrosarcoma. Average age of presentation was 30 years and male to female ratio was equal. Mandible to maxilla distribution was 4:3. Average length of history was 6 months. One of the fibrosarcomata exhibited particularly striking features suggesting that it had arisen by malignant transformation of a pre-existing benign fibroma. The tumor presented as a exuberated fleshy mass covering the lower molar teeth and extending on both buccal and lingual sides.

Malignant Ameloblastoma: was seen in a 45 years old female. It involved right maxilla in her. The patient presented with swelling of right upper jaw of 3 years duration and pain in the same jaw for 2 years. X-ray (PNS) showed radiolucent lesion of maxilla with multiple septae in between.

Dhaliwal[7] in his study of 231 cases of tumors of jaw found one case of malignant ameloblostoma involving lower jaw of a 25 years old female presenting with swelling of one year duration. Slootweg and Muller[12] in a review of literature found 20 cases (11 in females and 9 in males). Age ranged from 6 to 54 years, with mean age of 31.3 years, however they found 18 cases had mandibular involvement.

Osteogenic tumors: There were three patients with osteogenic tumors. These included two non-neoplastic lesions (fibrous dysplasia and giant cell granuloma). Third patient had a neoplastic lesion with a diagnosis of chondrosarcoma.

Chondrosarcoma was seen in a 100 years old male involving his right maxilla who presented with swelling of jaw of four months duration, bulging of right eyeball and recurrent epistaxis of 3 months duration. X-ray (PNS) showed a radiopaque shadow of right maxillary antrum with destruction of its walls. On histopathological examination the tumor consisted of sheets of densely packed cells and innumerable rudimentry blood vessels. Cells showed plump nuclei, more than one nucleus and hyperchromatism. Anand[1] in his review of 256 patients of jaw tumors in West Africa found a solitary tumor of chondrosarcoma in the mandible of a 41 years old man with a 4 months history. He found four patients of fibrous dysplasia and five patients with giant cell reparative granuloma.

Fibrous Dysplasia: was seen in a 43 year old female who presented with swelling and pain of left lower jaw of two months duration. On examination she had swelling of left ramus of mandible, 4x3 cms. size and firm in consistency. X-ray mandible showed a radiolucent shadow of ramus of the left mandible. Clinical behaviour of our patient is consistent with those of other studies in literature.[13,14]

Giant cell reparative granuloma: The lesion was seen in a 45 year old female who presented with swelling of left lower jaw intraorally of 2 months duration. She was unable to chew food on the same side. The patient had a swelling of 6x4 cms. size, firm in consistency. X-ray of the mandible showed a unilocular radiolucent shadow in the body.

Anand[1] in a review of 256 patients of tumors of jaw found four patients of giant cell lesions, however, the age of presentation was much younger than our patient, the average age of presentation being 12 years. Distribution of lesion between two bones was equal, male to female ratio was 1:3 and average duration of symptoms was 1½ years, much longer than our patient.

Dhaliwal[7] in 12 cases of reparative granuloma found nine patients were females while only three were males. Age ranged from 09-58 years.

Epithelial Jaw Cysts: Six patients of jaw cysts were encountered, three were radicular and three were dentigerous. Two patients with dentigerous cysts were in 3rd decade of life while the 3rd one was in 4th decade of life. Male to female ratio was 2:1. Two patients had involvement of mandible. The third patient had involvement of maxilla and both the lesions of the mandible were associated with unerrupted 3rd molar tooth. Our results are consistent with those of Shear[15] who in a study of 206 dentigerous cysts found 63.6% in 3rd to 4th decade of life, median age of presentation being 36.6 years. Males were 62%, females were 38%, 66% of cysts involved mandible, 34% were in maxilla and 69% of those in the mandible were associated with third molar teeth.

Mourshed[16] in a survey of 176 cases of dentigerous cysts found 61.3 percent occured in males and 38.7% in females, 74% occured in mandible and 69% of them involved the third molar area. The results are consistent with our study although we had less number of patients.

In all the three patients x-ray showed a unilocular radiolucent shadow with well defined sclerotic margins encircling the crown of an unerrupted tooth.

The inflammatory odontogenic cysts found in our series were three radicular cysts. All the three patients were in 2nd decade of life with two patients being males while one was a female. Two patients had involvement of maxilla, one had mandibular involvement Shear[15] in review of 1345 jaw cysts found 50% of them to be radicular, greatest number of cases occured in 2nd decade of life. 58 percent affected males and 42 percent affected females and 60 percent occured in maxilla. Our results are consistent with it. Radiological picture showed a rounded radiolucency with sharply defined sclerotic borders surrounding root of involved tooth. Two patients had no symptoms while one had swelling and pain because of infection of cyst.

UNCLASSIFIED LESIONS:

Carcinomas: Sixty five patients had a diagnosis of carcinoma comprising 70% of patients in our series which is different from those of Dodge,[3] and Anand.[1] Dodge found only 35 cases of carcinoma of Jaw in 117 patients of jaw tumors in Uganda Africa comprising about 10 percent only however, they had higher number of Burkitt's tumour of jaw which are rare in this part of the world. Our results are consistent with those of Dhaliwal who found 135 cases of carcinoma in an analysis of 231 tumors of jaw comprising 53 percent. On the basis of histopathological appearance various carcinomas seen were as under:

01. Squamous cell carcinoma: There were 56 patients who had sq. cell carcinoma. 40 patients had involvement of maxilla or maxillary antrum while sixteen patients had mandibular involvement with age ranging from 25-60 years. Maximum patients were seen in 5th and 6th decade of life. Results were similar to those seen by Dodge and Dhaliwal,[3,7] Anand[1] found 135 cases of malignant tumor of jaw out of which 102 were Burkitt's tumour which is not found in our region and there were 25 cases of carcinoma of jaw. 20 cases had involvement of paranasal sinuses, average age of presentation was 49 years. Maxilla was site of involvement in 14 and frontoethmoid in six patients. In 5 patients the site of involvement was buccal mucosa, average age of presentation was 45 years, male to female ratio was 4:1. Nearly all tumors arising in para nasal sinuses had reached a gross and often

grotesque stage, in their unbridled growth involving the orbit, palate or protruding from the nostrils.

Adenocarcinoma: This type of carcinoma was seen in four patients. All the four had involvement of upper jaw. Age ranged from 35 to 65 years with a male to female ratio of 3:1. All patients presented with swelling of cheek.

Anaplastic Carcinoma: Three patients had anaplastic carcinoma. All the three were males of the age of 40, 60 and 100 years and had involvement of maxilla.

Other lesions: There were five patients in this group, two had rhabdomyosarcoma. One had malignant melanoma and other two were schawanoma and an epulis.

Rhabdomyosarcoma were seen in a 9 month and a 9 year old child, both were males and both had involvement of maxilla. Presenting features were swelling of the upper jaw and dribbling of saliva. Rhabdomyosarcoma is a highly malignant soft tissue sarcoma of infancy and childhood, head and neck being a favoured site.[17]

Malignant melanoma was seen in a 50 year old male who presented with history of nasal obstruction and epistaxis. X-ray PNS showed a radiopaque shadow of left maxillary sinus with destruction of its medial wall. Histologically it had spindle cell and epitheloid components with distinct packeting. Small amount of melanin were present. Nuclei were large with prominent nucleoli.

Subbuswamy[2] found two cases, of melanoma in a study of 200 cases of oral and maxillo-facial tumors in Northern Nigeria. However, the age group was much younger than our patient, age being 10 years in both patients, one a male child and another was a female child. Dhaliwal[7] found a single patient of malignant melanoma in a study of 231 tumors of jaw.

Schwanoma was seen in a 35 year old male presenting with swelling of upper jaw, nasal obstruction and epistaxis.

Fibrous epulis was seen in a 23 year old female presenting with swelling of left upper jaw intraorally arising from gingvobuccal sulcus. Subbuswamy[2] found 13 cases of epulis in a study of 200 cases of jaw tumors. We saw only one patient probably because most of patients with this benign lesion would have attended dental hospital of the state.

Table-I: Distribution of 93 Jaw Tumors (WHO Classification)

S.No.	Type of tumors	No. of cases
01.	**Odontogenic lesions**	14
	a. Benign	
	i) Ameloblastoma	08
	ii) Ameloblastic fibroma	01
	b. Malignant	
	i) Fibrosarcoma	04
	ii) Malignant ameloblastoma	01
02.	**Osteogenic tumors**	03
	a. Neoplastic lesions (chondrosarcoma)	01
	b. Non-neoplastic lesions	
	i) Fibrous dysplasia	01
	ii) Giant cell granuloma	01
03.	**Epithelial cysts**	06
	a. Developmental	
	i) Nondentogenic	
	ii) Odontogenic cysts	03
	b. Inflammatory cysts (Radicular)	03
04.	**Unclassified lesions**	70
	a. Carcinomas	65
	i) Sq. cell carcinoma	58
	ii) Adenocarcinoma	04
	iii) Anaplastic carcinoma	03
	b. Other lesions	05
	i) Malignant melanoma	01
	ii) Epulis	01
	iii) Rhabdomyosarcoma	02
	iv) Schwanoma	01
	Total	**93**

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Increasing Incidence of Organophosphorus Poisoning in Kashmir Valley (a preliminary study)

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Abstract: *The study was conducted to have a preliminary review regarding increasing incidence of organophosphorus poisoning (OPP) in Kashmir Valley. The study on 164 patients evaluated the clinical profile (clinical manifestations, regional distribution, precipitating cause of consumption, outcome etc.) of OPP. The poisoning was predominantly reported in female (69.51%) and majority of patients (74.39%) consumed the poison for suicidal intentions, mainly due to strained social relations (precipitated by the prevailing turmoil). Ingestion was the commonest route of exposure (85.34%) and gastrointestinal symptoms predominated the clinical profile. Majority of the cases (70%) belonged to the districts having largest areas of apple orchards. Majority of patients (94.51%) recovered from the poisoning. Overwhelming use of organophosphorus compounds as insecticides/ pesticides and prevailing disturbances in the valley for last 8 years has led to an alarming increase in the incidence of organophosphorus poisoning.*

Key words: *Organophosphorus poisoning, suicide, gastrointestinal, insecticides/pesticides.*

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Introduction

The first highly potent organophosphorus compound (OPC) of anti-cholinestrase series tetraethyl pyrophosphate (TEPP) was synthesized by Clermont in 1854[1]. Toxicity of such OPC led Scherader to explore these compounds for insecticidal activity and as warfare agents. The annual consumption of various pesticides has been estimated by United Nations Agricultural Organisation in various countries (Table I)[2]. The latest estimates from WHO indicate that one million serious accidental poisonings and two million suicidal attempts invovling pesticides occur each year world wide.[3]

It has been estimated that over 50,000 OPCs have been synthesized and screened for insecticidal potency so far, of which over 3 dozen have been produced commercially.[1] Organophosphates poison the nervous systems by irreversible inhibition of cholinesterase-catalysed breakdown of the neurotransmitter acetylcholine. OPC thus cause stimulation of muscarinic receptors at autonomic effector organs; stimulation followed by depression or paralysis of all autonomic ganglia and skeletal muscles (Nicotinic effects) and stimulation with subsequent depression of cholinegic receptor sites in the CNS. The toxic effects of OPC on muscarinic receptors are blocked by atropine while as nicotinic effects are blocked by pralidoxime, OPC get absorbed through skin, lungs, gastrointestinal tract.

The various muscarinic effects of OPC include miosis, urination, diarrhoea, diaphoresis, lacrimation, excitation of CNS, salivation (best remembered by acronym Muddles). It also includes nausea, vomiting, abdominal cramps, increased bronchial secretions, bradycardia, conduction blocks and pulmonary oedema. The nicotinic effects consist of fatiguability, generalized weakness, involuntary twitchings, scattered fasciculations, hypertension, tachycardia and repiratory muscle paralysis. The various CNS effects of OPC include confusion, ataxia, slurring of speech, areflexia, chyene-stockes respiration, generalized convulsions, coma.

The most serious non-cholinesterase related effects of OPC is delayed neuropathy presenting 7-14 days after exposure. Recovery of neuropathy takes 6-12 months. This is thought to be due to inhibition of neuropathy target enzyme by some of OPCs[4]. An

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intermediate syndrome caused by few OPCs occurs within 24-96 hours after recovery from acute chlinergic crisis and consists of involvement of cranial nerves and proximal muscles and recovery occurs in 4-18 days[5-7]. Many OPC are also associated with irritation of the skin and upper respiratory tract. These compounds give rise to characteristic irritant symptoms and can also provoke nonspecific symptoms such as headache and nausea. Most of irritation is confined to upper airways but occasional complaints of wheezing and chest tightness have been reported.[2] The major cause of death from OPC is respiratory failure of pulmonary oedema.

Material and Methods

A total of 164 patients of both sexes, residents of different districts of Kashmir division of the J&K State presented to a Medical Unit in Casualty Department of SMHS Hospital, Srinagar with History of Exposure to OPC from April 1994 to July 1997 in a prospective randomized study. A thorough history regarding the type, quantity, duration, motive behind the exposure and symptoms of toxicity of OPC was taken. A detailed clinical examination was performed. A meticulous and adequate therapy was initiated in all patients and patients were subjected to different investigations in the form of Haemogram, KFT, LFT, Serum electrolytes. ECG and CXR. The gastric aspirate obtained after stomach wash was sent to chemical analysis in some patients. The red cell and plasma cholinesterase estimation and urinary toxin estimation could not be done due to lack of such facilities in the institution.

Observations

This study comprised 164 patients, 114 (69.51%) females and 50 (30.49%) males who were in the age group of 14-58 years. Majority of cases (74.39%) had consumed OPC for suicidal intentions, while at 25.61% took it accidentally and there was no case of homicide (Table-2). Majority of patients (46.34%) belonged to district Pulwama followed by district Baramulla 22.56% (Table 4). In Baramulla district 75% of cases were from Sopore Tehsil. Majority of patients (55.49%) had exposure to Dimecron whereas nature of OPC consumed was not known in 13.41% of cases (Table 2). More than 90% of cases had consumed 5-50 ml of various OPC, whereas rest of the cases had consumed 50-150ml of the same. Majority of patients (>80) reported to our casuality within 2-4 hours of exposure. The most common route of exposure was ingestion (85.34%) whereas topical application for scalp pediculosis accounted for 10.39% of cases (Table 2). Accidental inhalation while spraying various insecticides in apple orchards was noticed in 4.27% of cases. The various signs and symptoms observed in these poisoning cases are depicted in table 3. Thirty eight patients (23.19%) denied consumption of OPC on admission (though they had clinical features of poisoning) but on subsequent recovery they confessed the ingestion of OPC. The various precipiting factors for suicidal consumption of OPC are shown in table 5 There were no hematological, renal or hepatic abnormalities on investigation.

Table I: Pesticide Consumption in various countries (estimated by United Nations Food and Agricultural Organisation)

Name of Country	Metric Tons Active Ingredients
Africa	
Algeria	9400
Cameroon	3900
Morocco	9400
Zimbabwe	4000
Asia	
China	2,40,000
India	72,000
Pakistan	5,600
Thailand	36,000
Korea	26,400
Malaysia	40,000
Kazakhistan	10,000
Uzbekistan	10,000
Europe	
France	1,10,000
Germany	30,000
Hungry	17,400
Italy	80,000
Russia	27,000
U.K.	31,000

Discussion

Organophosphorus compounds are overwhelmingly being used as insecticides, pesticides and fungicides in our Valley in the agricultural industry. A good population of our Kashmir is involved in fruit growing and handling and therefore are frequently exposed to various organophosphorus compounds. The prevailing unfortunate turmoil and disturbances in the Valley has caused great sufferings and mental trauma to common Kashmiri by one or the other way[8] and also the easy access to these OPC have contributed to an increasing incidence of organophosphorus poisoning in the valley.

Table-2: Characteristics of Organophosphorus Poisoning Cases (n=164)

Characteristics	Number	Percentage (%)
Sex		
Males	50	30.49
Females	114	69.51
Age Group (years)		
14->25	55	33.54
25-<50	86	52.44
>50	23	14.02
Mode of Poisoning		
Suicidal	122	74.39
Accidental	43	25.61
Homicide none.		
Type of OPC		
Dimecron (phosphamidan)	91	55.49
Melathion	20	12.19
Dichlorvos (Nuran)	14	08.54
Tic-20	17	10.39
Unknown	22	13.41
Route of exposure		
Ingestion	140	85.34
Inhalation	07	04.27
Topical Application	17	10.39
Outcome of Poisoning		
Recovery	155	94.51
Deaths (mortality)	9	05.49

This study on 164 organophosphorus poisoning cases revealed the predominance of females in consuming these OPC. The major precipitating factor (in suicidal cases) in females was either failure in examination (Young girls) or strained social relations (Middle aged women) whereas major precipitating factors in male cases was failure in examination or inability to get good percentage of marks or frustration because of unemployement. Failure in love affairs, also contributed to suicidal consumption of OPC in both sexes.

Table-3: Signs and Symptoms observed in our organaphosphorus poisoning patients

Symptomatology	Number
Vomiting	139
Meiosis	128
Salivation	123
Incontinence	46
Diarrhea	64
Hypotension	28
Bradycardia	54
Pulmonary oedema	88
Respiratory paralysis	11
Fasiculations	141
Tachycardia	23
Hypertension	02
Convulsions	06
Coma	48

Table-4: Topographic Distribution of Oganiophosphorus Poisoning of Kashmir Valley (n=164)

S.No.	District	Number of Cases	Percentage (%)
1.	Pulwama	76	46.34
2.	Baramulla	37	22.56
3.	Budgam	18	10.98
4.	Srinagar	16	09.76
5.	Kupwara	9	05.49
6.	Anantnag	8	04.87

Tabl-5: Precipitating cause contributing to OPC Consumption in suicidal casses (n=122)

S.No.	Precipitating factor	No. of patients	Percentage (%)
1.	Strained social relations	37	30.33
2.	Failure in examinations	25	20.49
3.	Unemployment	22	18.03
4.	Failure in love affairs	17	13.93
5.	Unmarried pregnancies	9	7.38
6.	Psychiatric disorders	4	3.28
7.	Unknown	8	6.56

Topographically about 70% of cases were from Pulwama and Baramulla districts (especially from Shopian and Sopore tehsils). It could be because of increased use of organophosphorus compounds in these two districts which have largest areas of apple orchards and therefore, easy access to these compounds. The most common compound consumed was dimecron which is so frequently used as an insecticide. Since ingestion was the most common route of exposure to these OPC, gastrointestinal features of poisoning predominated in majority of cases. Other features like meiosis, fasiculations, diaphoresis, irritability, confusion were also present in large number of cases. But none of our patients developed inter mediate syndrome which has been reported with many OPC.[5,6] Though only two third of patients reported for follow-up, delayed neuropathy, which has been reported with organophosphorus intoxication[4] was not seen in any of these patients. The severity of symptoms and clinical outcome was directly related to the amount of poison consumed, route of exposure and the time interval between the consumption of poison and time of reporting to the casuality. By virtue of a meticulous and adequate management, majority of cases (including those who were comatosed or had pulmonary oedema, improved but 9 patients (5.49%) died. These were the cases who had either consumed large quantity of OPC, of those who reported very late to us or those who developed respiratory muscle paralysis before they could be shifted to the centre with facilities of ventilatory support. The psychiatric consultation in two third of the cases revealed underlying depression.

In conclusion, the incidence of organophosphorus poisoning is increasing at an alarming rate because of over-whelming use of insecticides, pesticides or fungicides, strained social relations (mainly precipitated by loss of a close relative in the prevailing turmoil), increasing magnitude of unemployment, frustrations about ones future, unstability in education, failure in examination, failure in love affairs and also because of pregnancies among unmarried girls, but meticulous and adequate management can save majority of precious lives. Further, proper psychiatric counselling can definitely avoid any future mishap in these subjects. Above all, let us hope that the people of this valley might come out of the prevailing turmoil, which would definitely decrease such mishaps.

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An Analysis of Vehicle Accident Injuries

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Abstract: The study comprises of a retrospective review of 378 vehicular trauma victims (7% of total craniocerebral traumas) managed at Sher-i-Kashmir Institute of Medical Sciences by the department of Neurosurgery from June 1994 to June, 1997. Patients were analysed by age and grouped as children (age <16 years), adults (16-59 years), or elderly (age >59 years). Overall children constituted 25.39% of patients, adults 59.52% and elderly 15.07%. Male: Female ratio was 2.85:1. Glasgow Coma Score (GCS) was the mainstay of assessment for neurological status. Commonest type of head injury was closed head trauma (42.85%). Commonest associated injury with head trauma was fracture tibia and fibula in adult group, fracture femur in children, and rib fracture in elderly age group. Surgery was performed on 26.98% of patients. The mortality rate was 9.52% with 52.7% deaths occuring during initial resuscitation measures.

To conclude, motor vehicle injuries have a distinct epidemiological feature in Valley of Kashmir and call for the need to improvise on accident prevention strategy.

Key words: Vehicle Trauma, Coma Score.

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Introduction

With more and more of urbanization and growing number of motor vehicles especially in an overpopulated developing country like India, the number of vehicular trauma victims is on the increase. Hence, a study of this pattern was undertaken which examines injury profile secondary to vehicle trauma, and analyse them for various age groups. The magnitude of the problem is more severe than reflected in this study, because it does not include cases of polytrauma admitted else where.

Methods

The medical records of all the cases of motor vehicle accidents admitted under department of Neurosurgery from June, 1994 to June, 1997 were reviewed.

Majority of the patients were kept under observation in the department of accident and emergency for 18-24 hours whileas patients with trauma to occipital regions were observed for 48-72 hours and discharged after ensuring hemodynamic stability and GCS-15. Only critically injured patients i.e. GCS<6 or hemodynamically unstable were shifted to Surgical Intensive Care Unit (SICU).

Results

A total number of 5,400 trauma victims of isolated craniocerebral trauma or craniocerebral trauma associated with other injuries were admitted under the department of neurosurgey at SKIMS, J&K, India from June, 1994 to June, 1997, out of which 378 cases (7%) were admitted secondary to motor vehicle accidents. The mean age of patients was 36 years (range 2 months to 85 years). Out of 378 patients 96 were children (25.39%); 225 were adults (59.52%) and 57 were from elderly age group (15.07%). Of 378 patients, 280 patients were male and 98 were female (M:F= 2.85:1). The types and number of injuries seen in our patient

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group is shown in Table-I.

Table-I

Showing Various Types and Number of Injuries

Part		No. of patients
A.	**Head**	**378**
i.	Closed head trauma	162
ii.	Skull fracture +	116
iii.	Extradural hematoma	28
iv.	Subdural hematoma	12
v.	Subarachnoid bleed	4
vi.	Intracerebral bleed	25
vii.	Facial trauma	16
viii.	Eye trauma	15
B.	**Extremities**	**80**
	Fractures of:	
i.	Tibia/fibula	30
ii.	Femur	12
iii.	Clavicle	10
iv.	Humerus	8
v.	Radius/ulna	7
vi.	Ankle	4
vii.	Multiple*	9
C.	**Chest**	**45**
i.	Rib fracture	25
ii.	Pneumothorax	8
iii.	Hemothorax	6
iv.	Multiple#	6
D.	**Abdomen**	**42**
i.	Liver	13
ii.	Spleen	10
iii.	Kidney	2
iv.	Bowel	3
v.	Mesentry	3
vi.	Multiple@	5
vii.	Diffuse tenderness	6
E.	**Pelvic fractures**	**26**
F.	**Spinal fractures**	**38**
	-Cervical	17
	-Dorsal	6
	-Lumbar	15

+ = include only isolated skull fractures.
* = who had fracture at more than one site.
# = who had more than one injury.
@ = who had multiorgan intra abdominal injury.

Intensive care monitoring in the surgical intensive care unit was required for 52(13.75%) patients, out of which 26(50%) belonged to the elderly age group (age> 59 years). The Glasgow coma score was significantly lower in elderly age group (Mean GCS = 8); followed by adults (mean GCS = 10) and children (mean GCS = 12). Since, the study was conducted on neurosurgical trauma patient, all 378 patients (100%) had head injury for which they were admitted and then evaluated for other injuries also. 110 patients (29.10%) had multiple injuries. The type and number of injuries are shown in Table I. When age-wise organ system analysis of injuries was done, extremity trauma was most common associated injury to head injury in children and adults, whereas pelvic fractures and rib fractures were mainly seen in elderly age group (see talbe II).

In head injury closed head trauma was the commonest type of injury seen in 162 patients (42.85%), followed by skull fractures in 116 patients (30.68%). Overall extremity fracture associated with head injury was seen in 80 patients (21.16%) out of which fracture of tibia/fibula was the commonest, seen in 30 patients, all of whom were from adult age group (age 16-59 years). 12 patients had fracture femur out of which 8 patients belonged to pediatric age group (age < 16 years).

Table-II Age-Wise Analysis of Injuries

	All patients		Pediatric		Adults		Elderly	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
No. of patients	378	x	96	25	225	59.51	57	15
Head injury	378	100	96	25	225	59.51	57	15
Extremity fracture	80	21	21	21	52	23	7	12
Chest injuries	45	11	8	8	29	13	8	14
Abdomen injuries	42	11	12	12	23	10	7	12
Pelvis	26	7	10	10	6	2	10	17.51
Spine	38	10	x	x	32	14	6	10.51
Multiple#	37	10	5	5	20	9	8	14

#meant any patient who had more than one system involvement as mentioned above.

102 patients (26.98%) were subjected to various surgical procedures as shown in Table III.

36 patients (9.52%) died during hospital stay out of which 19 patients died within 1 hour after admission, inspite of all resustative measures adopted. Mortality was significantly higher in elderly age group (14.03%). Most of the patients who died had GCS of less than 6 or multiple injuries of were elderly.

The majority of the accidents occured during summer months (May, June, July, August) and peak incidence was observed during office going and office coming hours i.e. 9a.m. to 11a.m. and 3p.m. to 5p.m.

Table III
Operative Procedures

Part	No. of patients
A. Neurosurgical	
I. Skull Operations	
i. Craniotomy/elevation of depressed fractures	30
ii. Evacuation of extradural haematoma.	28
iii. Craniotomy for drainage of acute subdural haematoma/ subacute subdural haematoma#	5
iv. Burr Hole drainage for subdural haematoma#	4
v. Craniotomy with evacuation of intracerbral haematoma	
a. Temporal haematoma	7
b. Frontal haematoa	6
c. Parietal haematoma	5
d. Fronto temporal	3
e. Fronto-temporoparietal	1
f. Parieto temporal	1
g. Parieto occipital	1
h. Bi-frontal	1
2. Spine	
- Cervical fusion	7
- Lumbar fusion.	7
B. Chest	
- Thoracotomy	3
- Chest tube insertion	9
C. Abdomen	
- Liver repair	13
- Splenectomy	7
- Splenorraphy	3
- Nephrectomy	1
- Small bowel repair	2
- Colostomy	1
- Repair of mesentric rents	1
- Negative exploratory laparotomy	4

#only 9 patients with subdural haematoma (acute, subacute and chronic) were operated. 3 patients with minimal subdural haematoma were managed conservatively.

Discussion

The study was undertaken with a specific purpose to know about the epidemiological importance of serious vehicular trauma.

Most of the series have shown considerable hemogenecity in sex-distribution, pattern of injuries, alcohol use and mortality rates.[1,2] Our study shows a definitive preponderance for male sex (2.85:1) and does not include any alcohol abuse.[9] The mortality of 9.52% is higher than 6% as reported by Kong et al[3] but is consistent with 6-30% of other collected series as reported by the said author.

Only 6.6% patients of the total number were subjected to laparotomy. Neurosurgical operations were the commonest type of surgery (70.66%), others report orthopaedic surgeries to be most frequent.[3]

Glasgow coma score was lower in the elderly age group and non-survivors. SICU admission rates were higher for elderly patients and the surgical outcome was poorer.[4,5]

Most of the accidents occured in summer months (May, June, July, August) and at the peak hours of the day and in urban areas, the reason being the heavy traffic on roads during summers and heavy pedestrian traffic at peak hours. We did not observe increased incidence towards week ends or night hours as reported by others,[2,6] because of the present political scenario in the valley.

Children and the elderly patients are prone to serious vehicular traumas, hence suggesting the importance of directed public health measures.[10,11]

Hence, we conclude that motor vehicle trauma has distinct epidemiological features in our valley especially in an urban population so necessitating the need for designing public health measures to decrease the incidence of these accidents which may be summarized as under:

1. Mass education programmes about traffic rules.
2. Children and elders should not be allowed to move alone on busy roads.
3. Use of crash helmets
4. Use of seat belts
5. Driving at slower speeds.
6. Avoidance of busy roads at peak hours.
7. Regular checking of automobiles.
8. Maintainence of roads, traffic signals and traffic signs.
9. Mass education about transportation of injured patients.

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Simultaneous Repair of Meningocele and Ventriculo-Peritoneal Shunt

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Abstract: *Simultaneous repair of Meningocele (MMC) and placement of Ventriculo-Peritoneal Shunt (VP shunt) was done in 20 children over a period of three years. All these patients underwent cranial ultasound preoperatively to detect the presence of ventriculomegaly. Nineteen patients are doing well with patent shunts and free of long term infections. The average post-operative stay was 3 days (range 3-9 days). We conclude that simultaneous repair of MMC and VP Shunt is an economic, safe procedure and avoids the risks of repeated anaesthesia and surgery.*

Key words*: Hydrocephalus, Meningocele, Shunt Infections, Spina Bifida, Cerebro-spinal fluid shunts.*

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Introduction

Hydrocephalus is common in patients with MMC and more than 80% of these eventually require a shunt, however, this is usually delayed.[5] Surgeons who are proponents of delayed shunt placements point out the likelihood of increased morbidity with simultaneous shunting, associated with long operative time, a higher incidence of shunt infection or malfunction and more importantly the need to document progressive hydrocephalus. However, going by the available literature, it appears that the results of simultaneous repair of MMC and VP Shunt are almost identical to that of delayed shunting.[1,4] The morbidity regarding the shunt infection and malfunction have also been low or equal in this series. Encouraged by experience of others[1,4], we started performing simultaneous repair of MMC with VP Shunt in children who had associated hydrocephalus proved by pre-operative cranial ultrasonography. The procedure has been found economic, safe, avoiding repeated trauma of surgery and risks of anaesthesia.

Patients and Methods

Twenty patients underwent simultaneous repair of encephalocele/meningocele and insertion of VP shunt from January' 1994 to April 1997. The age of these patients ranged from 2 weeks to 19 months. There were 5 neonates, 13 infants and 2 children below the age of 2 years. Ten patients had lesion in the occipital region, while lumbar and thoracic spine was affected in 7 and 3 patients respectively. All these patients underwent preoperative ultrasonography to document the presence of ventriculomegaly. Fourteen of these had obvious hydrocephalus, while 6 were found to have ventriculomegaly only after ultrasonography.

The operative technique for accomplishing simultaneous repair of MMC and placement of VP shunt was similar to that of Chadduck et al[2] in first 8 patients with some changes. The patient was operated in prone position with right side up. Unlike them, we didn't try intraoperative ultrasonography, magnification for neural tube closure and all the operations were done by a single surgeon at a time. In rest of the 12 patients we found that doing shunt first in supine position and later on changing the baby to prone position for excision and closure of MMC was more convenient. Antibiotics were started 12 hours before surgery and continued for 10 days postoperatively in all the patients. Patients were regularly followed every month initially and later every 3 months.

Results

Twenty patients with MMC and associated hydrocephalus underwent simultaneous repair of MMC and VP shunt. The average postoperative hospital stay was 3 days (range 3 to 9 days). The operative time was

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lengthened by 20 50 minutes because of the simultaneous placement of VP Shunt. One of these patients died 2 weeks postoperatively because of shunt infection and meningitis. Two patients had superficial infection of abdominal wound which settled by conservative treatment. However, all the surviving 19 patients are doing well with patent shunts and are free of long term infections. There was no cerebrospinal fluid leak from the repaired MMC.

Discussion

The conventional treatment of MMC has been closure of the lesion followed by delayed shunting if hydrocephalus develops later on. Eighty to 92% cases[1-6] require CSF shunt. However, this approach requires second admission for the patient and hence more expenses. Secondly, the case with border line hydrocephalus are at a risk of getting CSF leak after repair of MMC. Further more, the patient is also exposed to repeated trauma of anaesthesia and hospitalization. Recently, many surgeons have begun to perform one stage repair of MMC and placement of VP Shunt, if associated hydrocephalus is detected preoperatively. A series of 12 patients by Epstein et al[3], did not show any increase in morbidity or mortality in patients undergoing simultaneous versus delayed shunting in MMC with associated hydrocephalous. Similar and favourable experiences have been reported by others[1,2,4]. Our study also confirms the feasibility and safety of concomitant repair of MMC and insertion of VP shunt. We found that ultrasound is an important modality to detect the presence of ventriculomegaly and to aid in planning the treatment. In this series we found that 14 out of 20 patients had overt hydrocephalus, while 6 others were detected only by ultrasound. On the basis of these findings we can say that a normal head size in case of MMC cannot rule out the presence of associated hydrocephalus. The same observation has been emphasized by Stein at al[6]. Shunt infection is a persistent problem in any group of hydrocephalic patients and a shunt infection rate of 5-10% is not surprising.[6] A similar figure (5%) has been reported by Chadduck et al[2], in a comparative series of simultaneous repair of MMC and VP shunt versus delayed shunting. In our study, therefore, one infected shunt occuring among 20 patients (5%) doesnot appear excessive.

Based on the available literature and from this experience of 20 patients undergoing simultaneous repair of MMC and insertion of VP shunt, we believe that this approach has some advantages over the conventional delayed shunting. First of all, the patient is not subjected to repeated trauma of surgery and risks of anaesthesia. Secondly, the risk of postoperative CSF leak in patients with border line hydrocephalus is avoided. Further more, morbidity is less as evidenced by identical shunt infection rate[2,6], shorter hospital stay of patients and low hospitalization expenses of the procedure[2]. Finally, in children requiring multiple operations, it seems even more advisable to consider simultaneous shunting to minimize the delay of other necessary surgeries.[2]

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Paediatric Endoscopic Nasal and Sinus Surgery

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***Abstract** : Endoscopic nasal and sinus surgery has come to stay as a standard modality of treatment for Sinus disorders. We present our series of 18 children who underwent endoscopic nasal and sinus surgery during the past 3 years. The age of the patients varied from 7-14 years. All the patients tolerated the procedure well and there was no major complication. Followup varied from 3-30 months with a mean followup of 15.6 months. 87.5% of the patients showed improvement of symptoms from endoscopic sinus surgery. We conclude that endoscopic sinus surgery is a safe procedure in paediatric age group. Although this is a small series with limited followup, the early results appear to be encouraging.*

***Key words:** Endoscopic, Nasal and Sinus Surgery, Paediatric*

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Introduction

The development of Hopkin's rod system of endoscopes coupled with the introduction of Functional Endoscopic Sinus Surgery technique by Messerklinger[1] and Stammberger[2] has revolutionised the treatment of sinus disorders. The extension of Functional Ensoscopic Sinus Surgery technique to paediatric patients, although not new, is not practiced vigorously at all centres. The preliminary results from some centres have been encouraging. In this paper we have tried to evaluate our results of endoscopic sinus surgery performed on 18 patients of paediatric age group during the past three years.

Material and Methods

18 patients belong to paediatric age group constituted this study... After a detailed history followed by a thorough clinical examination, all the patients were subjected to a standard protocol of haematological and radiological examination (X-ray PNS Water's view). A diagnostic nasal endoscopy was performed in all the cases under local anaesthesia and sedation. CT evaluation of the nose and paranasal sinuses was carried out in 12 cases. Patients who, did not improve after a 2 week course of antibiotics were taken up for surgery. Along with endoscopic sinus surgery adenoidectomy, adenotonsillectomy and inferior turbinectomy was performed in one patient each to facilitate drainage and the nasal airway.

Technique

In 14 patients the procedure was performed under local anaesthesia and in 4 patients it was performed under general anaesthesia. Prior to operation the patients were under antibiotic and nasal decongestant spray. Those who underwent the procedure under local anaesthesia were premedicated with Inj. Pethidine hydrochloride and Inj. Promethazine hydrochloride as per their body weight. The nasal cavity was anaesthetised by 4% lignocaine by moffet's technique in 1: 100,000 concentration for 10 minutes. After infiltration with a local anaesthetic agent (2% lignocaine with adrenaline in 1:100,000 conc using a 27 gauge needle was done. The nose was then packed with 4% lignocaine with adrenaline (1: 50,000) for 5 minutes. The standard Messerklinger technique was employed. All the procedures were performed using 0^0 or 30^0 4mm telescope. The ethmoidal air cells were exentered, frontal recess opened, any polyp present was removed and the maxillary ostia were enlarged 3-4 times the normal size. In two cases sphenoidotomy was performed. During the surgical procedure, cottonoid soaked in high concentration of adrenaline (1:30,000) was used to achieve haemostasis. At the end of operation depomedrol is injected in to the cavity and packed with antibiotic steroid ointment. If there was excessive

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bleeding, a mercocel pack was placed in the cavity. Postoperatively the patients were put on a saline douch nasal decongestant drop, steroid spray and antibiotic for 10 days. One week after the surgery a nasal endoscopy was performed to clean the cavity of any clots, granulation tissue and remove any synechiae. At the end of it the cavity was again packed with steroid antibiotic cream. The patients were followed at weekly intervals initially, later on at fortnightly and monthly intervals.

Observations and Results

The age of the patients varied from 7-14 years with a mean age of 9.5 years. Males outnumbered the females by 2:1 (table 1) Table 2 shows the presenting symptoms and clinical findings. The findings of x-ray paranasal sinuses are depicted in Table 3 A diagnostic nasal endoscopy was performed in all the patients and the findings are shown in Table 4. Those patients who did not improve with antibiotic course, nasal decongestant and steroid spray were considered for surgery. A coronal CT of nose and paranasal sinuses was carried out wherever possible and the findings in 12 patients where CT was done are shown in Table 5. Patients were subjected to endoscopic sinus surgery and the various operations performed as well as the endoscopic surgery findings are shown in Table 6 and Table 7. The follow up period varied from 3 months to 30 months with a mean follow up of 15.6 months (table 8). The results were evaluated on the basis of improvement of symptoms. Out of 18 patients 16 would be evaluated and 2 patients were lost to follow up. 8 patients had fair to good improvement of symptoms, 6 had complete relief of symptoms and 2 patients had no improvement. There was no major complication. However 1 patient had bleeding due to injury to anterior ethmoidal artery which was treated by anterior nasal packing. 3 patients had synechiae and 3 others had meatal closure. (table 9).

Discussion

The treatment of chronic sinusitis in children by endoscopic nasal and sinus surgery is based on the fact that the larger sinuses are dependent on the pathophysiogical conditions of the anterior ethmoid complex i.e. Ostiomeatal complex. The diagnosis of sinusitis is based on the clinical manifestation and in children they include cough, rhinorrhoea and repeated upper respiratory infection.

Radiographic evaluation of the sinuses is of paramount importance in diagnosis and treatment in children by endoscopic sinus surgery. In children endoscopic sinus surgery should be comtemplated only when the patient does, not show any significant response to two week trial of antibiotics, steroid spray and nasal decongestants.

In children inspite of the anatomical variations, the authors have been able to successfully employ 4 mm telescopy for surgical procedure. Prior to sinus surgery, the surgeon must assess the status of adenoid, tonsils and inferior turbinates since hypertrophy of these may adversely affect the sinonasal physiology and contribute to recurrent or chronic infection of the sinuses.

The success of the surgical technique is based on excellant visualisation during the procedure for this it is mandatory to wait strictly for 10 minutes after applying vasoconstrictor packs in the nose. Post-operative management include putting the patients on antibiotics, nasal decongestants, saline douch and steroid spray. A nasal endoscopy is performed after 2 weeks of surgery under sedation and local anesthesia to remove any adhesions and crusts from the cavity.

The results of this series compare favourably with our earlier series[4] in adult patients as well as with that of other authors who have reported their results of paediatric endoscopic sinus surgery.[5,6] The safety of endoscopic surgery is demonstrated by lack of any major complication in this series. This series demonstrated that paediatric endoscopic sinus surgery can be safely performed if one follows the strict principle of proper patient selection and haemotasis during the procedure. The effectiveness of this modality of treatment is well demonstrated by improvement in symptoms.

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Treatment of Osteoarthritis, Rheumatoid Arthritis and Non-Specific Arthritis with a Herbal Drug: A Double-Blind, Active Drug Controlled Parallel Study

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Abstract: *The present study was conducted to assess the efficacy of Eazmov, a herbal preparation for treatment of osteoathritis, non-specific arthritis and rheumatoid arthrits in comparison with Diclofenac in a double blind randomised comparative parallel design model. Sixty adult patients of either sex were included in the study. Out of 60 patients 31 (16 Eazmov + 15 Diclofenac) patients were in osteoarthritis group, 17 (9 Eazmov + 8 Diclofenac) in non-sepcific arthritis group and the rest 12 (5 Eazmov + 7 Diclofenac) were in rheumatoid arthritis group. Eazmov or Diclofenace 50 mg was prescribed 1 Cap. thrice daily after meals for 6 months. Patients were assessed at baseline and then at 1,2,4 and at the end of 6 months of treatment. The herbal drug Eazmov has anti-inflammatory and analgesic activity as evident from the study in non-specific arthritis, reheumatoid arthritis and osteoarthritis. However, clinical efficacy was better, though not statistically significant. Side-effects profile, both clinical, hematological and biochemical were better with Eazmov than Diclofenac.From this study it can be concluded that Eazmov can be prescribed safely for mild to moderate joint pains and inflammations.*

Key Words: *Diclofenac, Eazmov, Osteoarthritis, Rheumatoid Arthritis, Non specific Arthritis.*

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Introduction

Osteoarthritis is a common progressive rheumatic disease characterised by degeneration and eventual loss of articular cartilage. It is the most common of the arthritis disorders and is the leading cause of joint pain in middle aged and elderly persons.[1] Presently, the nonsteroidal antiinflammatory drugs are the mainstay in treating this condition. However, they have serious adverse effects and have limitations for long term therapy.[2,3] The immunosuppressive drugs are reserved for rheumatoid arthritis as are the disease modifying drugs like the gold salts and cyclophosphamide.[4] Hence, there is a real need for drugs with good efficacy and a low toxic profile in the treatment of osteoarthritis.

A number of indigenous drugs have been claimed to be effective in the treatment of rheumatic disorders,[5] but their claims have not been substantiated in well controlled clinical trials.

A large number of herbal extracts are in vogue for the treatment of various types of arthritis.[6] Eazmov, a polyherbal anti-arthritic product from Indian herbs, Saharanpur, U.P., India, was reported to be significantly effective in different sets of anti-arthritic and anti-inflammatory experiment in domesticated and laboratory animals.[7] Significant reduction of the cotton pellet-induced granuloma in rats treated with Eazmov indicated the anti-kinin effect of this compound in the proliferative phase of inflammatory process.[7] Eazmov capsule contains *Cyperus rotundus, Tinospora cordifolia, Saussurea lappa, Picrorrhiza kurroa, Zingiber officiniale* etc. as extracts in their optimum concentrations.[8,9]

The present study was carried out to compare the efficacy of oral Eazmov capsule with Diclofenac in the treatment of osteoarthritis, non specific arthhritis and rheumatoid arthritis.

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Material and Methods

A parallel double masked comparative, randomised controlled clinical trial design was used. The study included 60 patients of osteoarthritis, non-speciic arthritis and rheumatoid arthritis. The patients of either sex and mean age of 53.6 ± 3.4 years attending the clinic were enrolled. The inclusion criteria were pain, morning stiffness, stiffness and/or joint swelling, disability and/or loss of function due to joint deformity with radiological changes. Patients with evidence of hypertension, diabetes, imparied renal functions, hepatic or cardiac dysfunction, pregnancy or nursing mother and women in the reproductive age groups, not practising contraceptions were excluded from the study. Informed written consents were obtained from the patients to participate in the trial and the study was approved by the ethical review committee. Identical vials with code number containing either Eazmov capsule or Diclofenac were supplied by M/s. Indian Herbus Research Supply Co. Pvt. Ltd. Saharanpur, U.P.

Dose and Duration of Study

Eazmov -1 capsule thrice daily after food/meal or Diclofenac -50 mg thrice daily after food/meal for 24 weeks in a double blind fashion.

Assessment of patients:

After selection, the patients were evaluated weekly for a pretreatment period of 1 months during which all their previous drug therapies were withdrawn. The patients were evaluated on a weekly basis during treatment using clinical parameters which included severity of pain (score), morning stiffness, Ritchie articular index, joint score as described by the American Rheumatism Association, disability score and grip strength.[10] Erythrocyte sedimentation rate (ESR) and radiological examinations[11] were performed every month. Side effects volunteered by the patients were recorded at each visit and the patients compliance was assessed by asking the patient to return the capsule container and counting the remaining capsules.

Formulation:

The indigenous formulation[12] based on Ayurvedic medicine was prepared from herbal materials, the composition of which is given in Table.1. The respective herbs were identified and tested for their quality. The good quality herbs were powdered and extracted with suitable solvents. The extracts thus received were standardised using modern analytical techniques (like TLC & HPLC) and mixed into desired quantities alongwith excipients which was suitably filled in hard gelatin capsules in accordance with standard guidelines described in Guide to good manufacturing practice.[12]

Observations were tabulated according to code and entered into the computer. a 'P' value of 0.05 was considered as the level of significance in all statistical tests. The analysis was done using programmable microstat package on PC-AT computer. The vials were decoded and then results were analysed. Differences between treatment groups were compared by the Wilcoxon and Student's 't'-test[13] Data were expressed as mean ± S.D.

Results:

Sixty patients completed this study and their demographic data and clinical characteristics on entry are given in Table 2. Out of 60 cases studied, 31 were of osteoarthritis; 17 were non-specific arthritis and 12 were rheumatoid arthritis. Out of 31 patients of osteoarthritis, 16 got Eazmov and 15 got Diclofenac. Out of 17 cases of non-specific arthritis, 9 got Eazmov and rest 8 got Diclofenac. Out of 12 cases of rheumatoid arthritis, 5 got Eazmov and rest 7 got Diclofenac. Treatment with Diclofenac or Eazmov for six months showed changes in favour of Diclofenac though not significantly different from Eazmov in maximum parameters (Table 3). Radiological assessment and ESR did not show any significant changes due to either drug. The side effect profile is shown in table-4. However, this side effects did not necessitate discontinuation of drug therapy. Patients compliance were satisfactory in both groups but the patients told that they were more comfortable with Eazmov.

Discussion:

The present study indicates the clinical, haematological and biochemical efficacy of the herbal drug "Eazmov" in the treatment of osteoarthritis, non-specific arthritis and rheumatoid arthritis. This formulation was designed after scrutiny of texts of Ayurvedic Medicine and available research data.[14] Tinospora cordifolia is considered to be efficacious [15]

This agent has documented anti-inflammatory and analgesic properties which should contribute to pain relief and a decrease in the inflammatory process. Its immunomodulatory activity couid alter the immunopathological processes rapidly and this may account for the beneficial effects observed in our patients. Picrorrhiza kurroa was probably added to protect the liver from noxious hepato-degenerative side effects of other ingredients.[15] It is evident from the result (Table 3) that there is definite improvement from pre treatment status to post treatment status in all the parameters like severity of pain, morning stiffness, Richie articular index, grip strength, disability score etc. in both Eazmov and Diclofenac. Treatment with Diclofenac significantly altered only the severity of pain ($P< 0.001$) and disability scores ($P< 0.05$). But effects with Diclofenac were more in comparison to Eazmov (Table-4). This might be due to proper formulation of different herbal ingredient to optimise theraputic effects and minimising side effects of each others. The exact mechanism of action cannot be commented on at this stage; however, the present study can be considered as an important step towards further research in order to understand more about the pathophysiology and treatment of these joint disorders. Herbal Eazmov appears to be effective and safe; however, its effect on long-term administration, remain to be evaluated in a larger sample group.

Acknowledgement:

The authors like to thank M/S. Indian Herbs, Sharanpur, UP for supply of the Eazmov and Diclofenac Capsule for the study.

Table - 1
Composition of Eazmov (Each Capsule of 400 mg contains the following ingredients)

Amrita	50 mg
Cleetnak	40 mg
Uashan	40 mg
Gundra	60 mg
Utpal	30 mg
Rohini	180 mg
Diluents	q.s.

Table - 2
Demographic Data of Patients on Entry (MEAN± S.D.)

Patients (n)	60
Age (years)	53.6± 3.4
Disease duration (years)	6.2±0.8
Sex ratio M/F	28/32
Body weight (kg)	62.5± 5.6

Table - 3
Effects of 6months Drug Therapy in Patients with Rheumatoid Arthritis, Osteoarthritis & Non-specific Arthritis

Criteria	Pretreatment Status		Posttreatment Status	
	Eazmov	Diclofenac	Eazmov	Diclofenac
Severity of Pain (Score)	3.78±0.94	3.68±0.71	3.27±1.12	0.94±0.61**
Morning Stiffness (minutes	122±20	118±12	120±18	108±13
Joint score (ARA)	4.75±0.17	4.82±0.24	4.30±0.86	2.90±0.26
Ritchie articular index (Units)	11.02±1.12	10.20±1.24	1.40±0.20	7.50±0.24
Grip strenght	16. 08±2.41	17.19±1.81	18.12±2.91	20.16±2.63
Disability	3.08±0.81	3.10±0.80	2.58±0.78	0.91±0.27*
ESR (mm/hr)	41.12±1.42	39.8±19	33.2±1.7	30.3±1.4

All values are Mean ± S.D. (n=60)

* $P<0.05$, ** $P<0.001$

Table - 4
Side Effect Profile of Eazmov and Diclofenac of 6 Months Study

Side Effect	Eazmov (n=30)	Diclofenac (n=30)
Number of patients with side effects	10(33%)	20(67%)
Total number of side effects	14	42
Most frequent side effects		
Abdominal pain	2	12
Asthenia	0	3
Fever	0	2
Headache	1	5
Digestive system overall	11	16
Dyspepsia	6	7
Anorexia	2	1
Flatulence	2	2
Nausea	1	4
Diarrhoea	0	0
Vomiting	0	2
Dizziness	0	2
Alopecia	0	1
Rash	0	1

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Attenuating the Cardiovascular Responses to Tracheal Intubation in Hypertensive Patients - A Comparison Between Metoprolol and Esmolol

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Abstract: *A randomized placebo controlled double blind study was conducted to compare the effects of bolus doses of metoprolol and esmolol on cardiovascular responses in hypertensive patients during laryngoscopy and endotracheal intubation (ETI). 60 controlled hypertensive patients of ASA class II received randomly placebo or the trial during (200 mgs of esmolol or 4 mgs of metoprolol in 20 ml of normal saline) 3 minutes before induction of anaesthesia. Heart rate, systolic and diastolic arterial pressure were recorded serially before induction, during endotracheal intubatin and one, three and five minutes after intubation. After decoding at the end of study the patients were grouped as Group I or placebo group, Group II or metoprolol group and group III or esmolol group. Statistical evaluation revealed highly significant (P<.0001) fall in heart rate, systolic and diastolic pressure at the time of endotracheal intubation and up to five minutes after intubation in group III as compared to group I. Group II also revealed a significant (p<.05) fall in these parameters compared to Group I which persisted upto 3 minutes following endotracheal intubation. A highly significant (p<.001) fall in heart rate was observed in Group III when compared to group II. Thus it was concluded that the use of bolus dose of esmolol 200 mg before induction of anaesthesia is effective in attenuating cardiovascular responses to laryngoscopy and endotracheal intubation and is comparatively better than metoprolol in hypertensive patients.*

Key Words: *Esmolol; Metoprolol; Heart rate; Systolic pressure; Diastolic pressure; Laryngoscopy and Endotracheal intubation.*

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Introduction

The frequent occurence of cardiovascular reactions to laryngoscopy and tracheal intubation has attracted the attention of anaesthetists for more than forty years.[1] The pressor response to laryngoscopy and endotracheal intubation (ETI) in the form of tachycardia, hypertension and arrhythmia after this routine procedure of modern anaesthesia, may be potentially dangerous.[2] These changes in blood pressure and heart rate have been seen to be associated with rise in plasma-noradrenaline concentration confirming a predominantly sympathetic response during intubation.[3]

Several efforts have been made to prevent these hemodynamic responses to laryngoscopy and intubation. These include maintaining deeper planes of anaesthesia, local instillation or systemic administration of lignocaine, narcotic analgesics, and use of vasodilators.[4,5,6] Beta adrenoceptor and anatagonists have been used to inhibit the reflex sympathoadrenal discharge which follows tracheal intubation.[7] Much attention has been given to use of selective beta adrenergic blocking drugs to prevent the reflex sympathoadrenal discharge mediated tachycardia and hypertension during laryngoscopy and endotracheal intubation and these include metoprolol[8] and more recently esmolol.[9]

Esmolol is an ultra short acting "cardioselective" beta adrenergic antagonist. Its major action is on sinus node function. It prolongs sinus cycle length but has no intrinsic automaticity.[10] It has a short plasma half life of 9 minutes.

The present study was designed to evaluate and compare the efficacy of metoprolol and esmolol when given in bolus doses on cardiovascular responses to laryngoscopy and endotracheal intubation in hypertensive patients.

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Material and Methods

60 patients of either sex, in the age group of 40 to 65 years with ASA class II, undergoing different elective surgical procedures under general anaesthesia were taken up for the study. Patients with uncontrolled hypertension and those already on Beta-blockers for hypertension or IHD were excluded from the study.

All patients received 10 mgs of diazepam orally at bed time the night before surgery and 5ug/kg buprenorphine I/M one hour before surgery as premedicant. In the operating room, an intravenous line was established, following which radial arterial cannulation was done under local anaesthesia for beat to beat blood pressure monitoring. Continuous EKG and blood pressure monitoring was done using space lab. monitor. Patients were randomly allocated to one of the three groups. Group I comprised 20 patients and received bolus dose of 20 ml of normal saline three minutes before induction of anaesthesia and served as control group; Group II comprising the same number of patients, received bolus dose of 4 mgs of metoprolol; Group III comprising same number of patients received 200 mgs of Esmolol in 20 ml of normal saline as bolus dose. Three minutes after the administration of the drug, patients were induced with intravenous thiopentone sodium 5mg/kg of body weight followed by intravenous suxamethonium bromide 2mg/kg. Laryngoscopy and endotracheal intubation was performed 90 seconds after the administration of suxamethonium bromide. Heart rate including any rhythm disturbance and blood pressure was recorded before induction, during and after laryngoscopy and intubation at zero, one, three and five minute intervals respectively. During the study period no other drug or inhalational anaesthetic agent was used as well as no surgical intervention was allowed. All patients were ventilated with 70% N_2O in oxygen using Bain & Spoerel coaxial circuit during the study period. Statistical evaluation of the data was done using students 't' test.

Results

The mean age and weight of the three groups was comparable. Percentage ratio of male and female patients studied was 45% and 55% respectively. The mean heart rate before induction was 91.40±10.69, 86.45±10.77 and 94.15±19.17 in group I, II & III respectively. The mean heart rate during laryngoscopy and endotracheal intubation in the three groups was 108.30±10.51, 94.95±7.49 and 83.40±6.50 respectively. The mean heart rate at 1 minute, 3 minutes and 5 minutes after endotracheal intubation in the three groups is shown in Table I. The fall in heart rate in group II as compared to group I was statistically significant ($p<0.01$) at one minute and at three minutes after ETI, where as the observed values were highly significant ($p<0.001$) during laryngoscopy and ETI, however the discrepancy observed before induction and five minutes after ETI was of insignificant value. When group I was compared with group III, there was a statistically highly significant ($p<.001$) fall in heart rate during, one minute, three minutes and five minutes after ETI whereas the variation before induction was of insignificant value.

Table I. Changes in heart rate (beats/minute) at various instances in group I, II and III

Stage	Group I Mean±SD	GroupII Mean±SD	Group III Mean±SD
Before induction	91.40 ±10.69	86.45 ±10.77	94.15 ±19.17
During laryngoscopy and ETI	108.30 ±10.51	94.95 ±7.49	83.40 ±6.50
1 minute after ETI	105.15 ±15.44	91.95 ±6.67	82.20 ±6.69
3 minutes after ETI	98.20 ±10.07	81.55 ±6.38	90.35 ±6.88
5 minutes after ETI	95.20 ±8.24	90.25 ±7.27	78.40 ±6.31

The variation in heart rate in group II as compared to group III, the readings observed were highly significant ($p<.001$) during, one minute, three minutes and five minutes after endotrachheal intubation where as the values were of insignificant value before induction of anaesthesia.

The mean systolic blood pressure before induction in the three groups was 131.80±12.34, 134.06±12.17, 138.65±14.12 respectively, while as during laryngoscopy and endotracheal intubation the readings in group I, II and III were 161.45±20.70, 148.55±12.23 and 139.25±19.09 respectively. The systolic pressure readings at 1 minute, 3 minutes and 5 minutes after ETI is shown in Table II.

The variation in systolic arterial pressure in group II as compared to group I, the readings observed during laryngoscopy and ETI was significant ($p<0.05$); whereas the variation was not significant at pre-induction, one minute, three minutes and five minutes after ETI.

The variation in systolic arterial pressure in group III as compared to group I, the reading observed during laryngoscopy and ETI and one minute after ETI were statistically significant ($p<0.01$). However, the discrepancy observed at preinduction, three minutes and five minutes after endotracheal intubation was of insignificant nature.

Table II. Changes in systolic arterial pressure (mmHg) in Group I,II,III

Stage	Group I Mean±SD	GroupII Mean±SD	Group III Mean±SD
Before induction	131.80 ±12.34	134.06 ±12.17	138.65 ±14.12
During laryngoscopy and ETI	161.45 ±20.70	148.55 ±12.23	139.25 ±19.09
1 minute after ETI	147.85 ±17.76	140.75 ±13.15	132.25 ±16.37
3 minutes after ETI	134.30 ±10.08	137.00 ±12.56	131.30 ±15.81
5 minutes after ETI	132.10 ±9.72	131.55 ±10.09	129.85 ±14.79

The variation in systolic arterial pressure in group II as compared to group III the readings observed at all instances was statistically insignificant.

The diastolic arterial pressure before induction in group I, II and III was 81.85±6.64, 81.75±5.43 and 81.80±7.67 respectively while as during laryngoscopy and ETI the readings in the three groups were 105.55±12.77, 89.80±5.49 and 89.75±10.98 respectively. The diastolic arterial pressure readings at 1 minute, 3 minutes and 5 minutes after ETI are shown in table III.

Table III. Changes in Diastolic arterial pressure mmHg in Group I, II, III

Stage	Group I Mean±SD	GroupII Mean±SD	Group III Mean±SD
Before induction	81.85 ±60.64	81.75 ±5.43	81.80 ±7.67
During laryngoscopy and ETI	105.55 ±12.77	89.80 ±5.49	89.75 ±10.98
1 minute after ETI	95.05 ±11.72	86.15 ±5.76	81.25 ±8.72
3 minutes after ETI	86.65 ±5.95	81.40 ±4.93	80.40 ±8.51
5 minutes after ETI	85.25 ±6.14	80.10 ±4.54	80.55 ±9.60

When group II was compared with group I the readings observed during laryngoscopy and ETI were highly significant ($p<0.001$), where as the variation was significant ($p<0.01$) one minute, three minutes and five minutes after ETI. However, the discrepancy observed before induction was of insignificant nature.

The variation in diastolic arterial pressure in group III as compared to group I, the readings observed during and one minute after ETI were highly significant ($p<.001$) whereas the variation was significant ($p<0.05$) at three minutes after ETI. However, the discrepancy observed before induction and five minutes after ETI was statistically insignificant.

When group II was compared to group III, the reading observed one minute after ETI was significant ($p<0.05$) whereas the variation was of insignificant nature before induction during two minutes, three minutes and five minutes after ETI respectively.

Discussion

Stress response under anaesthesia has been universally recognised phenomenon. It may occur in the form of endocrine or autonomic disturbances. The autonomic disturbances include haemodynamic responses to laryngoscopy and ETI during which, there is release of catecholamines[3]. The hemodynamic responses are deleterious for patients with hypertension, myocardial insufficiency or cerebrovascular disease.

Pyrs-Roberts (1973) used proctolal (0.4mg/kg) orally and intravenously and found that the patients who received beta blockers showed significantly attenuated responses of tachycardia and hypertension following laryngoscopy and ETI[2]. Denlinger et al (1974) used topical lidocaine 4% to produce surface analgesia of larynx and trachea and showed that it effectively blunted the increase in heart rate and blood pressure associated with laryngoscopy and ETI[12]. Robert Stoelting (1979) used rapid IV injection of sodium nitroprusside and found it effective to attenuate the stress response to laryngoscopy and ETI[13].

In the present study the mean heart rate showed a highly significant (<0.001) rise in group I patients during laryngoscopy and ETI as compared to preinduction levels and a significant rise ($p<0.01$) in group II and a significant fall ($p<0.05$) in group III as compared to preinduction levels. Group II and III showed a highly significant ($p<.001$) fall in heart rate during laryngoscopy and ETI as compared group I. In comparsion to group III, group II showed a highly significant ($p<0.001$) rise in heart rate during and at 1, 3 and 5 minutes after ETI.

Our results were comparable with that of Coleman and Jordan (1980)[8] who found a significant ($p<0.05$)

fall in heart rate at the time of induction with metoprolol. Our results correlate with the study of Oxorn et al (1990)[9] who have reported a significant ($p<0.01$) fall in heart rate following intubation with esmolol. Patients given 200 mgs of esmolol intravenously before induction, Sheppared Shane et al (1990)[14] who also reported same results.

The average levels of systolic pressure showed a significant fall ($p<0.01$) in group III patients when compared with group I patients during and one minute after ETI, whereas the fall was significant ($p<0.05$) during ETI only in group II patients. While comparing group II and group III patients the changes in average levels of systolic arterial pressure at different instances of study were significant.

In group II patients there was a highly significant ($p<0.001$) fall in diastolic arterial pressure during ETI only when compared to group I. There was significant rise in diastolic pressure only at 1 minute after ETI in group II when compared to group III patients.

The average diastolic blood pressure showed a highly significant fall ($p<0.001$) in group III as compared to group I during 1 minute after ETI and significant ($p<0.05$) fall at 3 minutes after ETI.

Oxorn et al (1990)[9] did not observe any significant changes in systolic and diastolic pressure following ETI after giving a bolus dose of esmolol 200 mgs IV before induction of anaesthesia since they conducted the study on non hypertensive, healthy patients whereas in our study, controled hypertensive patients were taken, who were hemodynamically more labile.

Our results were comparable to Coleman and Jordan (1980)[8] who did not observe any significant changes in systolic and diastolic pressure following ETI in patients given Metoprolol 4mg before induction.

Our results were also comparable with the study of Sheppared et al (1990)[14] who reported a significant decrease in systolic and diastolic blood pressure after ETI, when given 200 mgs esmolol intravenously.

We conclude that the use of esmolol as a bolus dose of 200 mgs before induction of anaesthesia is effective in attenuating the haemodynamic responses to laryngoscopy and ETI, and is comparatively better than metoprolol in this regard. Therefore, we recommend the use of esmolol before induction of anaesthesia for attenuating the cardiovascular responses to laryngoscopy and endotracheal intubation, particularly so, under the circumstances where these changes are highly undesirable like hypertensive patients.

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Prevalence of Psoriasis in Kashmir

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***Abstract:** An analysis of a total of 20988 patients attending Dermatology O.P.D. during 1 year period revealed that 689 subjects (2.4%) had psoriasis. About 60% of Psoriatic patients were males and about 40% were females. About 73% patients were in the age group of 11-40 years. Urban and rural subjects were 60 and 40 percent respectively. Religious pattern corresponded to it's general population pattern.*

***Key words:-** Psoriasis, Prevalence, Analysis.*

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Introduction

Psoriasis being one of the oldest recorded skin diseases, was first described by celsus as early as 35-40 AD[1]. Its prevalence in general population varies from 0.1% to 2.84%[2], but could be as high as 4.8% as in Norway[3]. Seen all over the world, it has a maximum prevalence in North Europe and North American population[4] and much less in oriental Jews[5]. It is more common in Parsees than Muslims or Hindus[6]. It is much less common among American Negroes[7] and exceedingly rare in American Indians[8] and Japenese[9].

The prevalence of psoriasis in North India amongst skin patients varies from 0.8%[10] to 1.4%[11].

Psoriasis displays a remarkable seasonal variation with high rate of onset in summer, though the condition is less severe in summar than winter[12].

It is reported to occur with equal frequency in males and females[13,14,15], Tendency for females to get the disease early than in males is well documented[12,15,16].

Patients with family history of psoriasis tends to have an earlier age of onset[16,17]. Prevalence of psoriasis is 3 times more in children of patients with onset of psoriasis before 15 years age than in those with age of onset above 30 years[18].

Material and Methods

Present study was intended to find out the prevalence of psoriasis in Kashmir. For this purpose one years data from Oct. 1987 to Sept. 1988 was analysed. This revealed skin O.P.D. of S.M.H.S. Hospital affiliated to the Medical College (which is the only centre to give a specialists cover of Dermatologhy patients in the whole valley and thereby caters virtually the entire population of the valley), of which 689 patients had psoriasis. Age and sex distribution is revealed in Table-I.

Table-I

Age and Sex Distribution

Age in Years	Male	Female	Total	%age
1-10	16	12	28	4.06
11-20	62	51	133	19.30
21-30	122	69	191	27.70
31-40	97	81	178	25.80
41-50	60	45	105	15.20
51-60	33	10	43	6.20
61-70	8	2	10	1.40
71-80	1	-	1	0.40
Mean Age	35	34		

Discussion

This indicates that even though the age ranged from 1-75 years, maximum patients (72.8%) belonged to the age group of 11-40 years. About 60% patients were males and about 40% females. Mean age for males and females being 35 and 34 years respectively. About 60% patients came from urban and about 40% patients from rural areas. Religious distribution amongst Muslims, Hindus and Sikhs was 92.4%, 5.90% and 1.5% respectively.

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One hundred and twenty psoriatic patients were picked up at random from amongst 689 patients of psoriasis for detailed a clinical history and examination and also were subjected to some metabolic tests. To assess the severity of the disease these patients were classified into 4 grades. Grade I subjects having skin involvement of less than 25% (28 patients), grade II with less than 50% (66 patients), grade III with an involvement of less than 75% (22 patients), and grade IV having over 75% skin surface involvement (4 patients). Thus maximum number of patients had grade II psoriasis and only 4 had exfoliative psoriasis. Family history of psoriasis was available in only 5 patients (4.16%). This group of 120 patients also revealed itching in 50 (41.6%), nail involvement in 45 (37.5%), photosensitivity in 17 (14.16%), mucosal involvement in 16 (13.3%), joint involvement in 1 (0.83%) and diabetes mellitus in 2 (1.6%) patients.

Comments

Many epidemiological studies based on population surveys have revealed great variations in the prevalence of psoriasis from 0.25%[9] in Japan to 4.8% in Norway[3]. Present study based on hospital out patients attendance shows a prevalence of 2.4%, 2-3 times higher to comparable studies in North India[10,11]. Psoriatic patients in Kashmir mostly belong to an age group of 11-40 years (72.8%) with a mean age of 34 years for females and 38 years for males compared to 19.34 for females and 36.9 for males in North India[11]. A sex ratio of 60:40 between males: females in the valley is comparable to a male preponderance ratio of 2.5:1 reported by Bedi[10]. Equal male and female involvement has also been reported[13,14,15] though female preponderance has been reported by Hellgren[12] Farber and Nail[15] and Holgate[16].

Family history of psoriasis was available in 4.1% in present study compared to 7.4% reported in North India[11]. Assessment of the extent of body involvement in present series revealed that 55% patients had grade II psoriasis involving 25-50% body surface compared to 75% patients with rural population revealed a 3:2 ratio of psoriasis in the valley where as the religious distributiuon roughly corresponded to their general population pattern.

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CASE REPORTS

Benign Intracranial Hypertension and All-Trans- Retinoic Acid

Gangadharan V.P.; Prakshh N.P.; Elizabeth Somini Koshy

Abstract: Benign intracranial hypertension (BIH) with all trans-retinoic acid (ATRA) in patients of Acute promyelocytic leukemia (APL) in adults is poorly documented. We report a case of BIH in an adult APL patient treated with ATRA.

Key words: Benign intracranial hypertension, All trans-retinoic acid, Acute promyelocytic leukemia

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Introduction

Benign intracranial hypertension (BIH) is a diagnosis of exclusion characterised by a syndrome of intracranial hypertension without clinical, neuro-radiological and laboratory signs of an intracranial space occupying lesion or of an infective process. Clinical presentation is variable with headache, nausea, vomiting and visual disturbances related to visual acuity and diplopia. Correlation of BIH with physiological (pregnancy, menarche), pathological or genetic conditions have been reported. Females are more commonly affected than males.[1,2] BIH of iatrogenic origin is particularly interesting and is frequent in the paediatric age. Retinoids, corticosteroids (therapy and withdrawal), tetracyclines fluroquinolones, amphotericin-B, nalidixic acid, nitrofurantoin, sulphamethoxazole, praziquantel, sulfenazone, acetyl salicylic acid, amiodarone, danazol, stanazol, oral contraceptives, lithium salts, leuprorelin acetate, have all been associated with this syndrome.[3]

ATRA (All trans retinoic acid) is a differentiating agent reported to induce complete remission (CR) in about 94% of patients of Acute promyelocytic leukemia (APL)[4]. It does not induce/worsen the APL coagulopathy unlike cytotoxic chemotherapy. ATRA is a safe drug with relatively few adverse reactions.

Though the association between BIH and retinoids is well known, the occurrence of BIH with ATRA in APL especially in adults is poorly documented. BIH as an adverse event with ATRA has been mainly described in paediatric patients treated for APL with dose of ATRA ranging from 45-80 mg/m^2/day[5,6]. We report a case of BIH in an adult APL patient treated with ATRA at Regional Cancer Centre, Trivandrum.

Case Report

20 years old female presented in August 1996 with one week history of fever and bleeding gums. She was pale with ecchymotic patches over trunk. Liver was palpable 2cms below costal margin and was non tender. Her hemogram revealed Hb 8gm%, WBC Count 21000/mm^3 and platelet count of 40,000/mm^3. Differential WBC count showed that 83% of cells were promyelocytes. Bone marrow examination confirmed the diagnosis as acute myeloid leukemia - M3 type (FAB). She had no evidence of DIC and her serum biochemical values were within normal limits. She was induced with ATRA for 30 days at a dose of 45 mg/m^2/day orally, along with supportive measures. On day 13, she developed headache, vomiting and right 6th nerve palsy. Optic fundi showed B/L papilloedema. CT scan brain and CSF study were normal. She was treated with mannitol, frusemide and analgesics. ATRA was discontinued for 7 days. There was no recurrence of the symptoms on reintroduction of ATRA. She achieved complete remission with ATRA and was followed up with consolidation chemotherapy. She continues to be in remission at 15 months follow up.

Discussion

ATRA is involved in three fundamental aspects of the development of the central nervous system[7,8,9]; stimulation of the axonal growth probably by a modulation of the response to nerve growth factor (NGF), migration of the elements of the neural crest, and specification of rostrum - caudal differentiation of

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the central memory system under development. But, to explain the pathophysiology of BIH, ATRA could be postulated as causing sluggishness of intra cranial venous circulation, slowing of cerebrospinal fluid absorption and causing hypo osmolar or vasogenic cerebral edema. This may be effected through changes in blood brain barrier, choroid plexus and arachnoid villi, the structures related to the production and drainage of cerebrospinal fluid.

Children are shown to be more markedly sensitive than adults to the central nervous system effects of ATRA. It could be a reflection of the variation in drug metabolism. An age related change in the RARS response to ATRA stimulating in the central nervous system, or a progressing age related reductions of RARS expression in the central nervous system[9] could also be postulated for this variation.

BIH is a diagnosis of exclusion and should satisfy the following diagnostic criteria[1,2,10]

1. Signs and symptoms of intra cranial hypertension
2. an awake and alert patient.
3. lack of localising neurological signs.
4. normally sized and shaped cerebral ventricles and lack of space occupying lesions on neuro imaging studies.
5. documented elevations of CSF pressure (200 and 250 mm of water, respectively in non obese and obese patients)
6. normal composition of CSF
7. No other detectable causes of intracranial hypertension.

Diagnostic approach includes physical examination and CT scan of brain. Lumbar puncture could be helpful to confirm diagnosis. Differential diagnosis include "isolated" headache, a common adverse effect of ATRA. "Isolated" headache is usually less intense, transient, well controlled by analgesics, and lack the other symptoms of raised intra cranial tension. BIH associated headache may be aggravated by analgesic or narcotic over use.[11]

The management policy of BIH with ATRA is still unclear. Symptomatic relief can be obtained with analgesic drugs like codeine or morphine sulphate. Temporary discontinuation of ATRA can be of help especially in non responding cases. Raised CSF pressure can be brought down with acetazolamide or frusemide. Lumbar punctures, with removal of CSF in order to maintain a CSF pressure less than 150 mm of water can be attempted.

Our patient had a dramatic relief of symptoms with Mannitol, and Frusemide along with codeine sulphate. ATRA was temporarily discontinued and restarted in the same dose after a gap of 7 days. The syndrome never recurred and she achieved a complete remission in 30 days treatment with ATRA.

Clinical trials[12] performed on adult's brain with higher doses (upto 150 $mg/m^2/day$) of ATRA for disorders different from APL did not show any evidence of toxicity on the central nervous system.[12] Further, reintroduction of ATRA is not shown to produce a recurrence of this syndrome, as is with our patient. Hence, can BIH be an association of APL, than an adverse reaction of ATRA?

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Intrabiliary Rupture of Hydatid Cyst

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Abstract: *In a consecutive series of 214 patients of hydatid cyst of the liver, 66 were complicated by intrabiliary rupture, being frank rupture in 28 and an occult communication in 38 cases. Abdominal pain, fever and jaundice were the common presenting symptoms and all patients had a palpable lump. The main diagnostic investigation were ultrasonography, radionucleide scanning, endoscopic retrograde cholangio pancreatography (ERCP), hydatid serology and the liver function tests.*

All patients were treated surgically. Cases with an occult communication were treated by evacuation of the cyst contents and the external tube drainage of the cyst while in case of frank rupture exploration of the common bile duct with removal of the parasitic debris and the daughter cysts was undertaken in addition to the external tube drainage of the cyst cavity itself. Common bile duct was drained by a T-tube in 12 patients and a choledochodudenostomy was undertaken in 16 patients. The average hospital stay for these cases was 20 days. The main post operative complications were wound infection, respiratory infection and cholangitis.

Key words: *Cholangitis, Choledochoduodenostomy.*

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Introduction

Hydatid disease of the liver is endemic in many parts of the World including the Middle East, Australia, Southern Europe, North Africa and parts of India. The surgery of the hydatid disease centres mainly on its complications and it is the onset of the complications that makes the morbidity not much inferior to that of the malignant disease. The most frequent complication is the intrabiliary rupture which has an incidence of 5-25%.[1-3] In 90% of the cases the communication between the hepatic hydatid cyst and the biliary tree may be occult. The cyst may be only bile stained and there is no demonstable communication on cholangiogram. In other cases the element of the cyst may drain frankly into the biliary ducts causing intermittent or complete obstruction of the common bile duct. Frank rupture requires exploration of the common bile duct and is treated by biliary drainage to prevent complication like cholangitis and biliary obstruction by the cyst elements.

The aim of this retrospective analysis is to outline our policy of the surgical management of 66 cases of intrabiliary rupture of hepatic hydatid cysts of the liver.

Material and Methods:

214 adult patients with hydatid cyst of the liver who were admitted in the General Surgical division of the Institute of Medical Sciences Srinagar during a thirteen year period from January 1983 to December, 1995. Sixty-six patients who had hydatid cyst complicated by intrabiliary rupture are reported here.

The main diagnostic investigations were ultrasonography; hepatic scintigraphy; X-rays of the chest and abdomen; casoni's intradermal test and ERCP. At surgery an upper right paramedian incision was commonly employed. During operation intra-operative cholangiography and injection of methylene blue into the common bile duct was used to demonstrate communication between the cyst and the biliary tree. All these patients had their cysts incised and evacuated of their contents and the residual cavitywas managed by external tube drainage in 56 patients in which the cyst cavity was infected. We employed omentoplasty to obliterate the residual cyst cavity in 10 patients in which the cyst cavity was non infected. Before incision, the cysts were surrounded by packs immersed in 2% formalin, some of the hydatid fluid aspirated and explored after injection of hypertonic saline. Whenever possible the openings of the biliary ducts into the cyst cavity were found and under-run with chromic catgut sutures.

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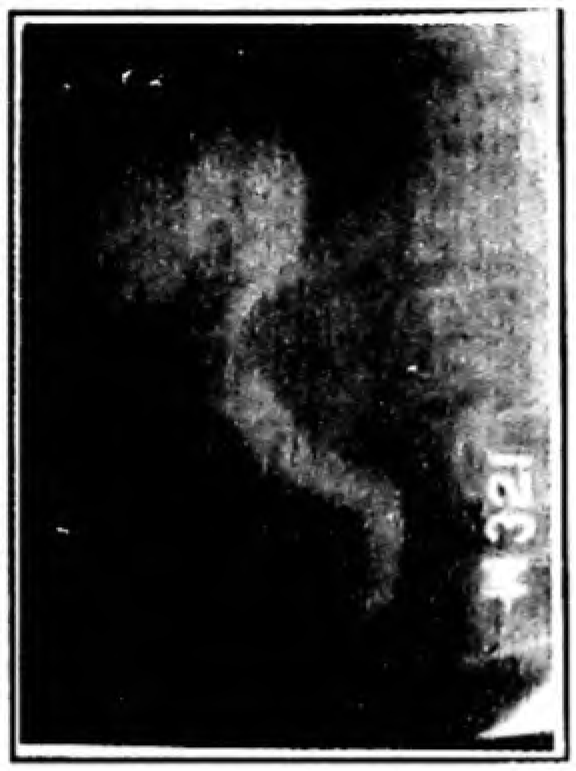
Common bile duct was explored in all cases of frank intrabiliary rupture. The common bile duct was drained by a T-tube brought to the exterior through a separate stab incision in the right flank in 12 cases. A wide choledochoduodenostomy was done in sixteen cases having gross dilatation of the common bile duct. None of the patients required a re-exploration. All patients with a T-tube were documented to have a free drainage into the duodenum before the T-tube was removed.



ERCP-Showing Hydatid cyst communicating with CBD and daughter cyst in CBD

Results

There were 24 male and 42 female patients. The age of the patients ranged between 20 to 60 years with a mean age of 40. The duration of the symptoms ranged from 3 months to 8 years.

The commonest symptoms and physical findings are shown in table-I. The most common symptoms were pain right upper abdomen, nausea, vomiting, jaundice, fever and rigors. The most consistent physical finding was an upper abdominal mass in all the cases; upper abdominal tenderness in 72% and hepatomegaly in 60% of the cases. Ultrasonography which was performed in all cases documented the presence of a cyst in all of them. CBD dilatation was documented by ultrasonography in all cases of frank intrabiliary rupture. Liver scan documented a filling defect in all 44 cases in which it was done. The main X-ray findings were elevation of the right dome of the diaphragm in 36 cases and a right sided pleural effusion in 4 cases. ERCP documented the presence of a hydatid membrane and an intrabiliary communication in fourteen of the sixteen cases in which it was undertaken.

Table- I
Symptoms and signs in 66 patients with intrabiliary rupture

Symptoms and Signs	No. of patients	Percentage
Pain	40	60
Fever	20	30
Jaundice	28	43
Rigors	36	55
Nausea/Vomiting	40	60
Anorexia	32	45
Upper abdominal mass	66	100
Upper abdominal tenderness	48	72
Hepatomegaly	40	60

At surgery liver enlargement was documented in most of the patients. Most of the cysts were located in the right lobe of the liver. The right lobe was involved in 48 cases and the left lobe in 18 cases. The diameter of the cysts ranged from 10-18 cms. The CBD was explored in all cases of frank intrabiliary rupture. The diameter of the choledochus ranged between 2-6 cms. During duct exploration daughter cysts, membranous debris and the purulent material was found in all cases. In 32 patients methylene blue was injected into the common bile duct and appeared in the cyst which identified the communication.

The average post operative period was 24 days. 36 patients had an uneventful recovery. The main post operative complication in respect of the patients were, wound infection in 20 patients and post operative pulmonary complications like atelectasis and pneumonitis in 10 patients.

Discussion

Hydatid disease is endemic in many parts of the World including India. Hydatid cysts of the liver causes pressure of the surrounding parenchyma and many cysts leak into a small duct or rupture into a large one.[4] The pressure inside these cysts is always higher than the pressure in the biliary tract and after rupture the cyst elements pass into the biliary channels. Apart from bile duct obstruction intrabiliary rupture of hydatid cysts leads to cholangitis, cyst infection and suppuration. In cases of frank communication, the right hepatic duct communicates in 55-60% and the left hepatic duct in 25-30% of the cases.[5]

A pre-operative diagnosis can be made in most cases by a detailed history, physical examination and the investigations. In an endemic area a patient having fever and rigors with jaundice and pain in the right upper quadrant of the abdomen with or without enlargement of the liver or a palpable mass should be regarded as a case of intrabiliary rupture of hydatid cyst until otherwise proved.[6,7] Ultrasound is a useful investigation as it shows the main cyst and the daughter cysts, the gall bladder and the common bile duct[8]. ERCP provides a safe and accurate pre-operative diagnosis and endoscopic sphincterotomy allows the patient to undergo elective surgery in a better condition after the suppurative cholangitis has settled[9,10]. Intra-operative diagnosis is very important when the pre-operative investigations do not reveal the communication. The presence of a dilated common bile duct with a liver cyst is indication for common bile duct exploration. Per-operative cholangiogram or injection of methylene blue should be done in every such case.

Machanism of Intrabiliary Rupture:

The pressure inside unruptured cysts was found to be 45-75 cm H_2O as compared to 25 cm H_2O of the biliary ducts. As the cyst grows it exerts pressure on the biliary ducts. One of the duct may get eroded and the contents of the cyst are partially evacuated into the ducts. Some of the contents pass into the duodenum but due to large amount of hydatid material generated from the mother cyst, the main duct ultimately tends to get blocked leading to obstructive jaundice and/or cholangitis.

The surgical treatment of a hepatic hydatid cyst complicated by intrabiliary rupture involves the management of the mother cyst and to manage the complication associated with rupture by exploring and draining the common bile duct. The mother cyst can be removed totally in selected cases but indiscriminate removal might result in haemorrhage and excessive bile leakage. The mother cyst can be opened; the parasitic elements removed and the cyst cavity drained by an external tube. Exploration and drainage of common bile duct is esential to avoid cholangitis and septic shock. Most authors like Lygidakis[3] and Dadoukis[5] advocate T-tube drainage as hazardous and insufficient[11]. T-tube is a source of infection into the biliary tree, causes loss of bile to the exterior, prolongs the hospital stay and thus increases the morbidity and mortality[12]. A T-tube provided only temporary drainage and after tube removal overlooked debris and the daughter cysts in the biliary tree can obstruct the duct. Alpher et al[11] have advocated and recommended a wide choledochoduodenostomy to reduce the morbidity and the mortality from intrabiliary rupture of hydatid cysts of the liver.

We did choledochoduodenostomy in sixteen patients and drained the common bile duct with a wide bore T-tube in twelve patients. Some authors have advocated cystojejunostomy in the treatment of intrabiliary rupture[13]. This technique, however, can only be used when the cyst has a mature wall and it only prevents external bile leakage. Even with this form of internal drainage the cyst elements may obstruct the biliary tree and cause cholangitis. Some surgeons have preferred sphincteroplasty to a choledochoduodenostomy[10]. However, sphincteroplasty is suitable when the common bile duct is of normal diameter. It has a higher morbidity and mortality rate as compared to a choledochoduodenostomy.

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Heterotopic Tissue in Gall Bladder

M. Saleem Wani M.S.; K.M. Baba. M.B.B.S. M.S.; K. Alam Wani M.S.

Abstract: Ectopic tissues are an unusual finding in Gall Bladder, we present a case of liver tissue found within the wall of Gall Bladder.

Key Words: Heterotopic Tissue, Gall Bladder

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Introduction

Heterotopic tissue in Gall Bladder is a well established yet a rare anomaly. Gastric tissue is the most frequent finding but adrenal, pancreatic, thyroid tissues have all been reported.[1] Ectopic liver tissue within the Gall Bladder wall (the most infrequent heterotopia) is presented.

Case Report

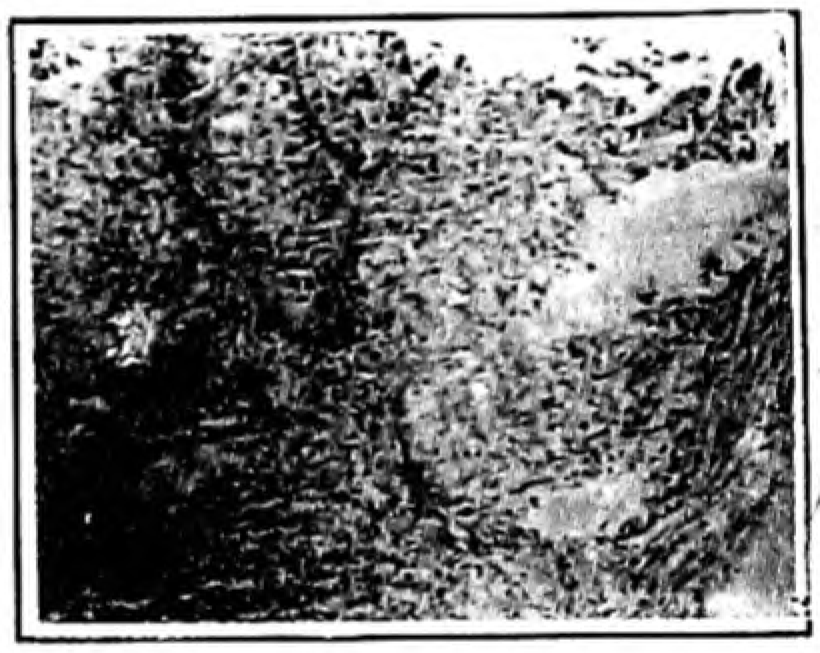
A 25 years old normotensive, nondiabetic female presented with recurrent right upper abdominal pain of five years duration. There was no history of fever, rigors, chills, jaundice, loss of appetite or upper gastrointestinal bleed. The physical examination of the patient was unremarkable. On abdominal examination there was no lump, organomegaly or ascites. Investigative profile of the patient revealed Hb of 12.8 gms%, TLC= 9.0x10$^{9/l}$, DLC = Polymorphs 72, Lymphocyts 26, Eosinophils 02. Kidney function tests and liver functon tests were all within normal limits. Ultrasonic examination of the abdomen revealed a distended gall bladder with multiple calculi and a mass measuring 3.25 x 2.15 cms at the neck of it. Common bile duct, intrahepatic ducts and liver was normal. Rest of the pelvic and abdominal ultrasound examination was normal.

Patient was operated with a pre-operative diagnosis of mass Gall Bladder with cholelithiasis, and cholecystectomy was done. The operative findings were as under:-

Gall Bladder distended and full. of multiple calculi with a firm smooth mass measuring 3x3 cms at the neck obstructing the cystic duct. Rest of the laporatomy was normal. Histopathological examination revealed features of chronic cholecystitis with liver tissues within the wall of Gall Bladder at its neck (Fig. No.1). Post operative period of the patient was uneventful and patient made full recovery.

Discussion

Heterotopic tissue in Gall Bladder is a well established yet rare anamoly. Gastric tissues is the most frequent finding but adrenal and thyroid tissues have been reported.[1,2,3] Pancreatic tissues which may include endocrine and exocrine elements have been reported.[2] Gastric body mucosa has also been seen, sometimes incontinuity with the mucosa of the Gall Bladder, some times deep within its wall. A multiseptate Gall Baldder containing thyroid tissue as well as gastric mucosa was reported in a 19 years female.[3]



Photomicrograph of gallbladder showing heterotopic liver tissue within its wall

Liver tissue is the most infrequent of all heterotopias. An acute acalculous cholecystitis is the most frequent mode of presentation, especially in patients less than 25 years of age. Heterotopia is nearly always accompanied by inflammation and cholelithiasis.[4]

In summary, heterotopias of Gall Bladder is indeed a very rare condition. Pre-operative diagnosis of this

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uncommon condition is extremely difficult as the condition closely simulates many other lesions giving rise to Gall Bladder mass. Histopathological examination of the cholecystectomy specimen can only lead to affirmative diagnosis of this condition.

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Agenesis of the Gallbladder

Ajaz A. Malik M.S.; Prof. N.A. Wani, M.S; FRCS; FICS

Abstract: *A case of agenesis of the gallbladder in a 45 years old female is presented who had a history consistent with cholelithiasis, and in whom oral cholecystography failed to opacity the gallbladder. The patient underwent abdominal ultrasound examination which was suggestive of gallbladder disease (cholelithiasis). Exploration revealed absent gallbladder with no evidence of any stones in the ducts or within the liver. The entity is discussed with reference to the review of literature.*

Key words: *Agenesis, cholecystitis, gallbladder.*

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Introduction

Agenesis of the gallbladder is a well recognised but uncommon congenital abnormality. Preoperative diagnosis of agenesis of gallbladder is impossible and therefore the usual diagnosis of this entity is made at laparotomy for suspected cholelithiasis on the basis of the clinical history and the failure of oral cholecystography to outline the gallbladder. Ultrasonography has revolutionised the diagnosis of biliary tract disease and proves helpful for diagnosing gallbladder disease in patients with non-opacification of the gallbladder on contrast radiology. However, the preoperative diagnosis may prove wrong on laparotomy by finding absence of gallbladder as has been observed in one of our patients. The biggest series of cholecystectomies in the world published from the Mayo clinic reported an incidence of 0.02%.[1] Rarity of this entity prompted us to report this case.

Case Report

A 45 year old female presented with a 2 years history of episodic right hypochondrial pain radiating through to her back without any fever or jaundice. Examination revealed mild tenderness in the right hypochondrium. Family history was not significant and there was no obvious congential anomaly. Barium meal and upper-gastrointestinal endoscopy were normal. An oral cholecystogram revealed non-visualization of the gallblader. Ultrasound of abdomen showed a doubtful gallbladder shadow containing gallstones. The patient was admitted for elective cholecystectomy.

At laparotomy, no gallbladder was found either in the normal subhepatic region or in any ectopic position. The common bile duct was of normal calibre and no stones were palpable therein. No calculi could be felt through the liver tissue. The reminder of the laparotomy was normal. The patient made an unevenful recovery and has been on followup for more than 1 year without any complaint. The calculated incidence at our centre is approximately 0.01%.

Discussion

Agenesis of the gallbladder was first reported in the literature by Lemery in 1701. Clinical cases have been reported more commonly in women.[2] The exact cause of the entity is not well documented but probably is either non-development of the gallbladder bud from the hepatic diverticulum of the foregut or a noncanalization of the bud.[3,4] A possible hereditary factor has been blamed in some patients of agenesis of gallbladder.[5,6]

The accuracy of diagnosis of gallbladder disease has improved since the advent of diagnostic ultrasound, CT scans and other imaging techniques. Gallstones are diagnosed best with ultrasound examination. However, the diagnosis of agenesis of gallbladder may be difficult on ultrasound as this entity is least thought of and only a few cases come in the life of an ultrasonographer to

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report such entity. Secondly, gas in the duodenum or in the hepatic flexure of the colon can produce echogenic areas with posterior shadowing and may mimic choleliathiasis[7], as possibly occured in our case.

The other imaging techniques for gallbladder disease such as technetium 99m, HIDA scanning, percutaneous transhepatic cholangiography and endoscopic retrograde cholangiopancreatography suffer the same deficiencies as oral cholecystography, in that failure to outline the gallbladder will be taken as indirect evidence of cystic duct obstruction. CT scan may allow the diagnosis of gallbladder agenesis to be made, but cannot be routinely used in this clinical setting.

When confronted, laparotomy with apparent agenesis of the gallbladder, one should exclude the possibility of the gallbladder at the ectopic sites, the intrahepatic gallbladder and the destroyed gallbladder as a result of repeated inflammation and only then a firm diagnosis can be made. In most reported cases of intrahepatic gallbladder, part of the organ can be visulised.[8] However, location of a rare, completely intrahepatic gallbladder can be made by palpation, needle aspiration or incision while as the intraoperative ultrasound may play a role in such cases. Intraoperative cholangiograph may reveal an intrahepatic gallbladder and will exclude other associated abnormalities of the biliary tree and choledocholithiasis.[2]

Exploration of the common bile duct has been advocated by some as a routine[2] while others have advised the exploration only on the abnormal intraoperative cholangiogram[9]. Agenesis of gallbladder may be associated with dilated common bile duct in some patients while calculi within a dilated duct are found in 25-50% of cases.[10]

It seems that most cases of agenesis of gallbladder will be diagnosed at laparotomy in patients with a clinical history suggestive of gallstones, who have had, in retrospect, equivocal evidence of cholelithiasis, while as the preoperative diagnosis will continue to present difficulties. More knowledge of the natural history of agenesis is required and a longer follow-up period for patients found to have agenesis of the gallbladder at operation would be helpful.

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Meckel's Diverticulitis Caused by Foreign Body

Nisar Ahmad Bhat M.S.; Mohd. Saleem Wani M.S; Sheikh Khursheed Ahmad M.S.;
Altaf Ahmad Shera M.S. M.Ch.

Abstract: Meckel's diverticulitis may occur denovo or may result from a foreign body in the diverticulum. We present a case of diverticulitis due to a foreign body (wooden piece).

Key Words: Meckel's diverticulum: Diverticulitis; Foreign body.

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Introduction

Meckel's diverticulum though seen only in 1 to 3% of the population[1,2], its complications are seen more frequently. One of the causes of diverticulitis is foreign body impaction and various foreign bodies have been identified to cause it.

Case Report

A three year old boy was admitted with chief complaints of abdominal pain for two days. Examination revealed tenderness in right iliac fossa. Haematological investigations revealed leucocytosis of 12,000 per cum; X-ray of the abdomen revealed a gas shadow in the right iliac fossa. At operation an actuely inflamed Meckel's diverticulum was found with a foreign body (wooden piece) incarcenated into it. The Meckel's diverticulum was narrow necked. Diverticulectomy was done. Post operatively patient made uneventful recovery.

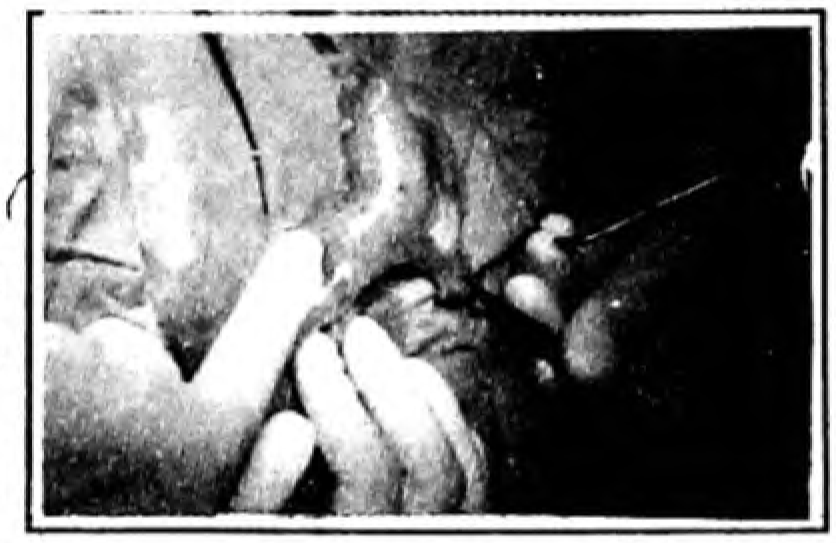

Fig. 1 Photograph showing inflammation of Meckel's diverticulum with foreign body

Discussion

As pointed out by Mayo[5] "Meckel's diverticulum is frequently suspected, often looked for and seldom found" However, diverticulitis is a recognized complication of Meckel's diverticulum and is reported to be the third most common complication[1,3]. In the case reported, lodgement of wooden piece led to the complication of Meckel's diverticulitis Rosswick reviewed 50 case reports of foreign body perforation of Meckel's diverticulum and no less than 28 of these were due to fish bones[6]. Other foreign bodies included a cherry stone, a knitting needle, a gramophone needle a wooden splinter and a chicken bone. Rutherford and Akers found three cases of Meckel's diverticulitis with perforation (two from peptic ulceration and one from a pine)[7].

Meckel's diverticulum can be identified pre-operatively by Nuclear scanning, baruim contrast studies, arteriography and occasionally by computed tomography with varying degree of success. The diagnosis is occasionally suggested on plain x-ray of the abdomen on the basis of an enterolith or a radioopaque foreign body in the right lower quadrant.

The management of Meckel's diverticulum found incidentally on laprotomy is controversial[3]. There is a general agreement that diverticulum that appears to have heterotopic mucosa on physical examination should be resected because of higher risk of subsequent complication[5]. Diverticulum with a narrow neck and with a foreign body within it should also be resected.

Wooden piece desected out from the diverticulum

In summary careful review of medical history and diagnostic aids should help in arriving at diagnosis of Meckel's diverticulum and its complications.

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Hodgkin's Disease of the Small Bowel-A Case Report and Review of Literature

Rather A. Rasheed, MD; R.P. Chisti, MD; Ruby Reshi, MD; G. Jeelani Romshoo, MD.

Abstract : Hodgkin's disease represents only a fraction of lymphomatous disorders orginating in the gastrointestinal tract. There is a paucity of information on this entity in literature which inspired us to report a case and review the literature regarding some salient aspects of small intestine Hodgkin's disease.

Key words: Hodgkin's lymphoma; Histiocyte; Reed-Sternberg cell.

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Case Report

A 33 year old young female pnor few weeks to admission had noted progressive weakness, a feeling of epigastric fullness, midepigastric pain and weight loss. The patients's past medical history and family history were non-contributory. The patient appeared clinically ill and a palpable tender, ill-defined intrabdominal mass was felt in the upper quadrant of abdomen. Investigations showed a haemoglobin of 9.8 grams/dl and a haematocrit of 36 volumes per cent. The white blood cell count was 12400/c mm with 76 percent Neutrophils and 24 percent Lymphocytes.

Radiological study including X-Ray chest and abdomen, Gastrointestinal series and Barium Enema were of no diagnostic value. However repeated stool examinations revealed a positive, haem-occult test.

Lacking a specific diagnosis, the patient underwent laparotomy. At operation the stomach and duodenum were normal and the liver was free of tumour. The jejunum was the site of apparent neoplastic involvement. The surgical specimen consisted of a 50 cm. segment of small intestine and its attached mesentery. The intestinal wall opposite to areas of serosal opacification was thickened and indurated. On opening the bowel, margins were thickened and indurated. Palpable within the mesentery were numerous small lymph nodes, the largest of which was 2x2 cm.

On microscopic examination the ulcerated lesions exhibited extensive destruction of mucosa and submucosa. The muscularis is was infiltrated by a variety of cells including small mononcleer cells, eosinophils, plasma cells and histiocytes. A few neoplastic cells with lobulated hyperchromatic nuclei and histocharacteristics of Reed-Sternberg cell were present. The stromal elements of bowel exhibited fibrinoid necrosis and fibroblastic activity. Sections of the enlarged lymph nodes revealed loss of architecture and replacement by similar cellular infiltrate.

Discussion

Lymphomatous disorders originating in the gastrointestinal tract comprise less than 4 per cent of lymphomatous disorders and Hodgkin's disease represents only a fraction of this group of diseases.[1] Hodgkin's disease of small intestive differs somewhat from Hodgkin's diseas of other parts of the gastro-intestinal tract as it is less likely to be associated with a generalized form of disease[2-6]. In our case also the neoplastic lesion was confined to jejunum only. Review of the clinical aspects of the published reports of this disorder indicate that the average patients first report symptoms in the fifth decade of life, but the range of age of onset is from thirty to sixty nine years and that Hodgkin's disease is evenly distributed between the sexes.[7] In one study of 51 cases of Hodgkin's Lymphoma, the youngest patient was an 11 year old girld and the oldest was a 76 year old woman (median age 42 years)[8].

In our case the patient was a young female of thirty

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years. The diagnosis of this condition is rarely made clinically and usually awaits surgical discovery. Examination may reveal a palpable abdominal mass, as it did in our case.[9-10]

Laboratory findings although not diagnostic sometimes implicates Lymphoma group, notable Hodgkin's disease as the source of the suspected gastrointestinal lesions. As in Hodgkin's disease of other organs a significant eosinophilia may be noted.[11]

Radiographic studies may suggest diagnosis if a small Bowel series demonstrates multiple ulcerating lesions separated by strips of normal mucosa and associated with dilatation and narrowing of the bowel lumen.[12] However in our case radiographic studies were non-contributory.

Histologically Hodgkin's disease of the small bowel manifests the same variability in the degree of fibrosis, cellularity, eosinophilia and number of bizzare histiocytes as does Hodgkin's disease of other organs.[11]

In diagnosing Hodgkin's disease the unequivocal identification of the Reed-Sternberg cell in its classical form is still regarded mandatory. However, the Reed-Sternberg cell has diagnostic specificity only if it is found in the context of an admiture of mononuclear, eosinophil and other cells which invariably produces some effacement of the affected tissue.[13]

The specimen in our also contained a mixed cellular infiltrate including Reed-Sternberg cells.

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Malignant Gastric Teratoma - A Case Report

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Abstract: *Gastric teratoma is an extremely rare tumour of infancy and childhood. In most of the reported series, tumors were benign. Malignancy in gastric teratoma is extremely rare. In this case report we present a 4 month old male child with gastric teratocarcinoma.*

Key Words: *Gastric, Teratoma, Teratocarcinoma.*

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Case Report

A 4 month old male child was admitted in Paediatric Surgery department of Sher-i-Kashmir Institute of Medical Sciences, Srinagar with progressive distension of abdomen of 1 month duration and history of malena of 15 days duration. Child was anaemic and had a marked abdominal distension with a mass of variable consistency occupying almost whole of abdomen.

Gastric teratoma arising from stomach

Plain x-ray of abdomen showed an area of calcification. Ultrasonography showed a mass of mixed echogenecity but exact anatomical location was not clear. Intravenous pyelogram was normal.

Exploratory laparotomy showed a tumour arising from posterior surface of the body of the stomach. Tumor had a small endogastric component as well. Tumor was excised including a margin of stomach wall.

Photomicrograph showing terato carcinomatous elements

Histopathology revealed teratocarcinoma (intermediate grade).

Discussion

The stomach is a rare site of origin for teratomas. Gastric teratomas account for <1% of all childhood teratomas and there is a marked male preponderance. As a rule gastric teratomas are benign and malignancy in gastric teratomas is extremely rare.

Our case is unique in the sense that the histopathological examination of the tumour revealed "intermediate grade teratocarcinoma" which is exceedingly rare and there is paucity of similar report in literature.

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PRACTITIONER'S COLUMN

Antiemetic Therapy in Chemotherapy Induced Emesis

Mushtaq Ahmad, MD;

Introduction

Nausea and vomiting are the most distressing and most feared side effects associated with administration of chemotherapy for neoplastic diseases. Optimal management of chemotherapy induced nausea and vomiting can be critical to the patient's quality of life. Nausea in particular often has been ignored in studies of chemotherapy side effects. Recently, progress has been made in control of chemotherapy- induced nausea and vomiting partly due to better understanding of the physiological mechanisms involved.[1] Further improved control of vomiting has come from better use of antiemetic agents by giving the drugs more frequently and at higher doses. With availability of new drugs in particular serotonin antagonists like ondansetron, granisetron and tropisetron significant gains have been made in controlling ematogenic side effects of cancer chemotherapy but controversies regarding the optimal and cost effective use of these agents have emerged.[2] Despite recent advances in antiemetic therapy, however, optimal management of chemotherapy induced emesis remains a challenge

Machanism of nausea and vomiting

The mechanism of nausea is not well understood. Nausea is mediated by the automonic nervous system and is accompanied by flushing, perspiration, pallor, gastric stasis and tachycardia. Retching and vomiting are, however, coordinated through the somatic nervous system. There are multiple afferent pathways of emetic reflex with potential role of numerous neurotransmitters. In early studies, two distinct areas of central nervous system, the emetic centre and the chemoreceptor trigger zone, appeared to mediate vomiting. The emetic centre is located within lateral reticular formation of the medulla oblongata and is not in itself sensitive to drugs. It receives input from number of afferent impulses including some from chemoreceptor trigger zone which is located in the area postrema in the floor of the fourth ventricle.[3] Recent studies in the ferret model suggest that the major site of antiemetic activity of 5-HT3 receptor antagonists is a vagal afferent terminals, although central vagal sites may also be involved. Since serotonergic neurons particularly of 5HT3 are found both in CNS and the periphery, they play key role in emetogenesis, induced by cancer chemotherapy. Ondansetron and other 5HT3 antagonists, therefore, hold promise to be effective antiemetic agents whereas metoclopromide being benzamide derivative is a D2 antagonist and a weak 5HT3 blocker.[4]

Chemotherapy induced emesis is usually classified as either acute, delayed or anticipatory. Acute nausea and vomiting usually occurs within 1-4 hours of treatment and may resolve within 24 hours. Delayed nausea and vomiting first occurs atleast 24 hours and sometimes even days after cytotoxic chemotherapy. Anticipatory nausea and vomiting is thought to be conditioned response provoked by such factors such as sight, sound and smell of the hospital or presence of chemotherapy nurse. It occurs before acute chemotherapy related symptoms would be expected to occur.

Factors determining the severity of emetogenesis

Numerous factors can influence the incidence and severity of nausea and vomiting. There are:

i. **Patients susceptibility to emesis**

ii. **Previous experience of drug induced emesis.** Anticipatory nausea and vomiting occurs approximately in 20-40% of patients during later

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cycles of chemotherapy.

iii. **Chemotherapeutic agent**

Cisplatin is severely emetogenic drug wherever bleomycin is the least emetogenic one. Table I shows emetogenic potential of various chemotherapeutic agents. Combination of chemotherapeutic agents is more frequently associated with nausea and vomiting than single drug.[5]

iv. **Dosage of Chemotherapeutic drug**.

The dosage and route of administration significantly affects the emetogenicity.

v. **Timing of administration**

Some studies show that timing of administration may influence the degree of emesis. Patients receiving chemotherapy in the evening report less degree of nausea and vomiting than those receiving during day time[6]. However these studies need to be further confirmed.

Management

There is considerable evidence that support the use of behavioral interventions in the form of relaxation techniques, distraction and hypnosis, reduce the post-treatment nausea and vomiting and prevents the development of anticipatory nausea and vomiting.[7]

Table I
Relative emetogenic potetial of chemotherapeutic agents

Severe	Moderate	Mild
Cisplatin	Mitomycin C	Bleomycin
Decarbazine	Doxorubicin (bolus)	Vincristine
Streptozocin	5-Fluorouracil (bouls)	Vinblastine
Carmustine	Cyclophosphamide	Daunorubicine
Procarbazine	Cytarabine	6-Meracaptopurine
		Melphalan
		5-Fluorouracil (influsion)
		Doxorubicin (infusion)
		Methotrexate

Adapted from Morrow (5)

Table II lists the major classes of antiemetics used. Phenothiazines have been used in the treatment of chemotherapy induced nausea and vomiting for more than 30 years. Their antiemetic activity is mainly due to blockade of dopamine receptors. Recently also in double blind crossover study, we reported high dose prochlorperazine is an effective antiemetic agent in cisplatin induced emesis.[8] High dose metaclopromide has also been documented in number of studies as an effective drug[4]. Combination of metoclopramide and dexamathasone appears to be particularly effective.[9] The mechanism by which corticosteroids act as antiemetic is not well understood.

The benzodiazepines especially lorazepam have been used in combination. It exhibits mild antiemetic activity and its anxiolytic and amensic properties can have beneficial effect on anxiety. However phenothiazines, benzamides, butyrophenones are associated with unpleasant antidopaminergic activity including akathisia, extrapyramidal reactions, anxiety and hypotension. Their widespread use has been limited by number of side effects.

A large step forward in control of chemotherapy induced emesis came with discovery of serotonin (5HT3) receptor antagonists. In this category granisetron, ondansetron and tropisetron are in clinical use.[10]

Table-2
Antiemetics used for chemotherapy-Induced Nausea and vomiting

Drug Class	Examples
Phenothiazines	Prochlorperazine; thiethylperazine
Butyrophenones	Haloperidol; droperidol
Sustituted benzamides	Metoclopramide
Corticosteroids	Dexamethasone; methylprednisolone
cannabinoids	Dronabinol
Benzodiazepines	Lorazepam; diazepam
Serotonin antagonists	Granisetron; ondansetron; tropisetron

In recently concluded study at our centre where high dose metoclopromide was compared with ondansetron, it was found antiemetic control was better with ondansetron in complete absence of sedation and extrapyramidal reactions. However effectiveness of ondansetron appears to be less for delayed nausea and vomiting. The addition of steriod such as dexamathosone increases the efficacy of both 5HT3 antagonists and other antiemetic agents. A direct comparison of all three serotonin inhibiting agents that is ondansetron, granisetron and tropisetron was reported in recent studies. All three 5HT3 receptor antagonists were effective in control of acute emesis. Different studies report efficacy of tropisetron and granisetron in delayed vomiting also.[10]

No double 5HT3 receptor antagonists have been proven to be more effective in control of nausea and vomiting but their optimal and cost effectiveness remains to be explored.

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HOSPITAL TODAY

Health into the Twenty-First Century

Syed Amin Tabish, MBBS, MHA, MAMS, FIMSA, FRIPH, MHSM

Most, if not all, countries all over the globe are striving to cope with health care transformations. Epidemiological and demographic transitions have resulted in an increase of chronic and degenerative as well as neoplastic diseases. Accompanying this trend is the re-emergence of communicable diseases. Improved life expectance has led to an increase in the number of people aged 65 and older. Development in information and communication technology have resulted in a better informed and more demanding populace. New technology and the expansion of scientific knowledge coupled with evidence-based medicine have resulted in changes to the way care and other services are provided. Persistent and/or increasing unemployment is leading to more poverty and poorer health. The universal trend is towards greater decentralization, pro-market economic policies, a rapid expansion of the private health sector, the introduction of charges to users and purchaser-provider splits, Developing countries like India are though still struggling to expand their health infrastructure and provide basic health facilities for all the population. If India is to progress towards equity, equality, comprehensiveness, universal accessibility and coverage, radical institutional reforms in the health sector are needed. Providing mechanisms for the delivery of essential cost-effective quality care is a government responsibility and of necessity, requires a strong sustained political will. The potential advantages from restructuring health care is that it can be extended to these who need it most. Recent experiences of developed countries suggest that investment, in decentralised population-based and health service research aimed at the developing evidence based health care, rather than the present emphasis on central, disease based system could yield substantial health gains for the population. There is growing concern about the problem of emerging and re-emerging infectious diseases and new diseases such as new srain of Cholera (Cholera 0139) and HIV infections which are the leading causes of morbidity and mortality. Diseases such as malaria, tuberculosis, Kalazar, dengue hemorrhagic fever, hepatitis A,B,C,D,E & G, Japanese encephalitis, rabies, and plague threaten the lives of millions of people. Some of the important factors contributing to the emergence of these diseases are rapid growth of population, unplanned urbanisation. disturbance of environmental balance, the increased speed and frequency of travel within and between countries, the low priority and support given to public health services, pollution, economic factors, educational level, and drug resistance on casual strains. India should develop effective warning mechanisms by improving its disease surveillence systems. This would have to be complemented by a rapid response mechanism. Prompt preventive and control measures is an absolute necessity.

The health services would be expected to be responsive to the needs of all; cost-effective and affordable and of high quality; humane, caring and culturally acceptable; innovative in its provision of services and exploitation of technology; sensitive to the wide spectrum of health from nuclear biology to socioeconomics and the environment; based on sound ethical principles that define individual responsibility as much as the state's obligations, and able to measure the outcomes of its investment.

World Health Organization has identified four priority areas for future action; ensure value for money. poverty reduction, public health policy, strengthening national capabilities for emergency relief and humantarian assistance. With each advancement in healthcare knowledge and technology, new skills are required to apply them. This situation may be offering

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the potential for new roles for classical categories of health professionals or the appearance of new categories. Care must be taken not to aggravate the imbalances of quantity-mismatch between the numbers a country needs and what it can reasonably offer, of quality-mismatch between the training and the job that needs to be done, and of distribution-mismatch between geographical, occupational, private/public, institutional and speciality mix.

The World Bank in its 1993 report proposed that in poor countries the focus should not be on complex, sophisticated, high technology care such as heart surgery, but on services that are essential. The report advocates the organization of health services into: essential clinical packages, containing, for example, treatment for tuberculosis, management of the sick child, neonatal and delivery care, family planning, treatment for sexually transmitted diseases, infection and minor trauma, assessment, advice and pain alleviation; and public health services, which include expanded programmes for immunization, school health programmes, tabacco and alcohal control, health, nutrition and family planning information, sexually transmitted disease prevention, monitoring and surveillance. These packages are estimated to cost low-income countries USD 8 and USD 4 per capita, respectively, but could result in reducing the equivalent of 7 million infant deaths a year. The delivery of the essential clinical and public health packages is estimated to require 1.0 to 2.0 physician per 1,000 population and between 2 and 4 qualified nurses per physician, or 10 to 20 physicians per 100,000 population and 20 to 400 nurses. The selection of the contents of the service is based on the burden of disease through an index referred to as DALYs-disability adjusted life years. DALYs measure the total loss of healthy life through premature death and disability.

More recently, increasing, concerns have been raised about the cost of health-care as well as value for money. These new concerns make it imperative for planners and policy makers to review the structure and compositon of healthcare organization and its workforce to ensure the most effective and efficient performance.

The World Health Organisation recommends at least 5 percent of GDP (on health care) if equality and universal coverage are to be raised. There is need to invest increasing proportion of resources in interventions that are known to be effective and where outcomes can be systematically monitored, and to reduce investment in interventions shown to be less effective. Investment must be made in improvement of health status, a national resource to which national governments should commit. The national government should reaffirm its commitment to the health of individuals, families, communities and the nation as a whole. National health policy needs to be formulated with particular emphasis on long-term and comprehensive strategies, attention to macroeconomic efficiency, based on the real health needs of the population, equity of access and financial burden, balance ongoing specialisation with the development of a strong primary healthcare sector, and encourage substitutability among health groups and facilitate the role of the family and the community. An essential requirement is a coherent link between national goals and strategy and implementation at the local level. This will enable achievement of national policy and establish a framework for managing change in the local health system. There is an obligation locally to create organisational structures and a culture that deliver accessible quality healthcare, facilitate building networks and create an effective work force.

The health sector therefore needs radical institutional reforms-In particular, improvements in functioning of public bureaucracies and a diversified approach to health services delivery. The objective, India is striving towards with such reform is to increase basic health services to underserved populations in the context of limited institutional capacity. While restructuring the health services, emphasis does however, need to be on decentralised decision making universal accessibility and coverage, self-reliance, intersectoral action for health, use of appropriate technology, consideration of cost effectiveness in relation to the available resources, and establishing of sound infrastructure. Emphasis is being given to raising awareness about health and enhancing public participation. Nevertheless, key areas of health development still need to be identified and in the pursuit of equality, special effort are required to reach the underprivileged, underserved are the renewed attempts to raise the quality of effectiveness of health services and rethinking of priority setting. Furthermore, competition in the supply of health services needs to be encouraged to improve quality and reduce diversity.

Although organising quality care for all citizens is a responsibility of government, the public have important responsibilities. The international community and individuals within it, can also contribute. The governments should assume leadership in initiating and managing change within their health systems, scrutinize all public policies for health implications and their application to the health of the community its health system and its health work force.

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OVERSEAS DIARY

The Educational Commission for Foreign Medical Graduates (ECFMG)

History :

In 1955, the Cooperating Committee on Foreign Medical graduates (CCFMG) was formed to evaluate graduates from foreign medical schools for entry into graduate medical education programs in the United States. On the recommendation of CCFMG, a private non-profit organisation known as the Evaluation Service for Foreign Medical Graduates (ESFMG) was formed in May 1956. The name was changed in December 1956 to Educational Council for Foreign Medical Graduates (ECFMG). In March 1958, ECFMG administered its first examination in 17 test centres to 298 graduates of foreign medical schools. The examination developed with the assistance of the National Board of Medical Examinees (NBME) consisted of a medical science examination and English language profinency test.

In 1974, ECFMG merged with the commission on Foreign Medical Graduates - the combined organisation was named Educational Commission for Foreign Medical Graduates, retaining the acronym ECFMG.

In 1996, ECFMG administered step1 and step2 of the United States Medical Licensing Examination (USMLE) in 79 test centres throughout the world to approximately 14,000 examinees per administration and issued standard ECFMG certificates to 12, 124 graduates of foreign Medical Schools. From July 1998, it is proposed to add a Clinical Skils Assessment (CSA), to the requirements for ECFMG Certification and some changes in the Medical ecducation credential policy are bound to be there.

Bearing a period for 1982 to 1989 the Indians are the largest recipients of ECFMG certificates right for 1969. More certificates were issued to citizens of India, 2570 (21.2%) than to any other country. China with 881 (7.3) certificates was second followed by U.S citizens, 750 (6.2%) who graduated from Medical Schools abroad.

Certification:

To be eligible for certification by ECFMG, graduates of foreign medical schools must meet the following requirements.

Pass the Medical Science Examination:

A passing score has to be achieved in both the basic medical science and clinical science test. Currently the ECFMG administers step 1 ans step 2 of United States Licensing Examination (USMLE) each step requires two days of testing. The examination is administered twice annually.

English Language Examination: The ECFMG english test is designed to assess proficiency in the comprehensive and line of the English language. It is a multiple choice examination, consisting of three sections : listening comprehensive; structure and written expression; and (non-medical) vocabulary and is adapted from the validated test of english as a Foreign Language (TOEFL). This test is taken by both Foreign National and US Citizen graduates of Foreign medical Schools.

Document the Completion of educational requirements: Documentation of completion of all educatioal requirements to practice medicine in the country in which the medical education is received is a must. Graduates of foreign medical schools must have had at least four credit years at the time of graduation in the World Directory of Medical Schools published by the World Health Organization.

Standard ECFMG Certificates :

Candidates who meet the medical examination and English language requirements, fulfill the medical education credentials requirements and clear their financial accounts with ECFMG are issued standard ECFMG certificates. The certificates remain valid for two years based on the date of passing the engligh test. Certificates that are not used for admission to residency programs prior to the certificates expiration date can be revalidated by passing on ECFMG english test of test of english as a foreign language (TOEFL)

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Source : Educational Commission for Foreign Medical Graduates 1996 Annual Report

ECFMG EXAMINATION CENTRES

EUROPE :

✦ FRANCE *(Paris)* ✦ GERMANY *(Frankfurt)* ✦ GREECE *(Athens)* ✦ HUNGARY *(Budapest)* ✦ ICELAND *(Reykjavik)* ✦ IRELAND *(Dublin)* ✦ ITALY *(Rome)* ✦ POLAND *(Warsaw)* ✦ SPAIN *(Madrid)* ✦ SWITZERLAND *(Geneva)* ✦ UNITED KINGDOM *(Liverpool, London)*

NEAR & MIDDLE EAST :

✦ ISRAEL *(Tel Aviv)* ✦ SAUDI ARABIA *(Riyadh)* ✦ TURKEY *(Ankara)*

AFRICA :

✦ EGYPT *(Cairo)* ✦ GHANA *(Accra)* ✦ SOUTH AFRICA *(Johannesburg)*

FAR EAST :

✦ HONG KONG ✦ JAPAN *(Tokyo)* ✦ PHILIPPINES *(Manila)* ✦ SINGAPORE *(Singapore)* ✦ TAIWAN *(Taipei)* ✦ THAILAND *(Bangkok)*

OCEANIA :

✦ AUSTRALIA *(Sydney)* ✦ NEW ZEALAND *(Auckland)*

NOTE : Availability of examination centres subject to change

SOURCE : Educational Commission for Foreign Medical Graduates (1996 Annual report)

Examinee Performance: ECFMG English Test and USMLE Step 1 and Step 2 Administered by ECFMG in 1996

	Step 1 June 1996		Step 1 October 1996		Step 2 March 1996		Step 2 August 1996		ECFMG English March 1996		ECFMG English August 1996	
	Number of Examinees	% Passing	Number of Examinees	% Passing	Number of Examinees	% Passing	Number of Examinees	% Passing	Number of Examinees	% Passing	Number of Examinees	% Passing
Total	**14,339**	**46.2**	**15,551**	**42.5**	**15,962**	**45.7**	**12,664**	**44.7**	**10,673**	**66.3**	**9,888**	**62.1**
	2,109	**42.7**	**1,601**	**31.7**	**1,028**	**31.7**	**1,273**	**46.7**	**545**	**90.8**	**732**	**91.0**
First Takers	**1,027**	**64.0**	**479**	**40.5**	**71**	**35.2**	**67**	**28.4**	**61**	**83.6**	**65**	**86.2**
Repeaters	**1,082**	**22.6**	**1,122**	**27.9**	**957**	**31.5**	**1,206**	**47.8**	**484**	**91.7**	**667**	**91.5**
	12,230	**46.8**	**13,950**	**43.7**	**14,934**	**46.6**	**11,391**	**44.5**	**10,128**	**65.0**	**9,156**	**59.8**
First Takers	**3,170**	**51.5**	**4,744**	**48.1**	**4,126**	**44.9**	**2,817**	**43.4**	**3,065**	**66.2**	**2,345**	**63.5**
Repeaters	**9,060**	**45.2**	**9,206**	**41.5**	**10,808**	**47.3**	**8,574**	**44.8**	**7,063**	**64.5**	**6,811**	**58.5**

Note: First Takers are those examinees with no prior ECFMG, VQE, FMGEMS, Part I and Part II, or Step 1 and Step 2 examination history.

Citizenship is as of the time of entrance into Medical School.

Statistics for each examination are as of mailing date of examination results and do not include incompletes or those for whom scores were withheld.

JOURNAL SCAN

Helicobacter Pylori Infection in Various ABO Blood Groups

This study was carried out to assess the prevalence of Helicobacter pylori infection in various ABO blood groups of people of Kashmir in Gastroenterology Deptt. (SMHS).

The study comprised 80 individuals- 50 peptic ulcer patients (whose disease was diagnosed by endoscopy) and 30 asymptomatic volunteers. Every subject's blood group and Rhesus status was determined by standard serological tests. Helicobacter pylori infection was diagnosed by three different methods viz., one minute endoscopy room test (urease test), Gram staining and by histology. The detection of Helicobacter pylori by histological examination using Giemsa staining was taken as the 'gold standard' for the presence of Helicobacter pylori infection. Out of 80 individuals, 67 were males and 13 females aged between 18-65 years. The majority of peptic ulcer patients had blood group 'O' (n=28.56%). The prevalence of Helicobacter pylori infection amongst peptic ulcer patients was 76%. There was no difference in Helicobacter pylori positivity in various blood groups. Blood group 'O' though a risk factor for peptic ulcer (Duodenal ulcer) is not a risk factor for acquiring Helicobacter pylori infection.

Source: Romshoo G.J., Bhat Y; Malik. G.M., Rather A.R., Naikoo. B.A., Basu J.A. Hussain. T., Samia R. Helicobacter pylori Infection in Various ABO Blood Groups of Kashmiri Population Diagnostic andTherapeutic Endoscopy, 1997; Vol.4, pp. 66-67.

Toxoplasmosis and Recurrent Abortions

In this study women with repeated abortions were secreened for prevalence of toxoplasma antibodies (IgM) to determine any possible aetiological relation between abortions and toxoplasma infection. The study included 285 women with repeated abortions and 169 control subjects. The number of pregnant subjects in the abortion group was 155 (54.38%) compared with 197 (63.37%) in the control group. The number of abortions ranged between two and five. Forty eight per cent of the abortions had occurred in first trimester, 36 per cent had occurred in second trimester, and 16 per cent had occurred in third trimester. Of 285 women with repeated abortions, 141 (49.47%) serum samples were positive of IgM toxoplasma antibody, two (0.70%) were equivocal, while 142 (49.82%) were negative. In contrast, only 15 (8,88%) serum samples were positive for IgM toxoplasma antibody in 169 controls. Thus seroprevalence of toxoplasma IgM antibodies was significantly more in women with repeated abortions than in control subjects.

In view of the high prevalence of Toxoplasma gondii in our subjects with repeated abortions it is recommended that every women in reproductive age who has history of abortion should be tested for her toxoplasma serological status before next conception and treated accordingly. Women with negative serological tests are at risk of acquiring a primary infection during pregnancy and education regarding preventive measures should be provided to them.

Source:- Zargar AH, Masoodi SR, Laway BA et al. Seroprevalence of toxoplasmosis in women with repeated abortions in Kashmir. J. Epidemiol Community Health 1998;52:135-136

Corticosteroids Cause Cataracts even by inhalation

Community based study with data collected during 1992& 1993 in Sydney (Australia) was undertaken, to determine the effect of inhaled corticosteroid use on the development of Cataracts in older adults. Patients completed questionnaires specifying inhaled corticosteroids use (currently, in the past, or never). Investigators categorised beclomethasone use for usual number of puffs/week and calculated the estimated lifetime dose. Other risk factors assessed were history of smoking, diabetes hypertension, socio-economic status and sun-related skin damage. The rates of posterior subcapsular, cortical and nuclear cataracts were 6%, 24%, and 19% respectively. The use of inhaled corticosteroids at any time was associated with in creased prevalence of nuclear cataracts and posterior subcapsular cataracts. Higher cumulative life time dose of beclomethasone was associated with increased prevalence of posterior subcapsular cataracts. Life time dose of beclomethasone >200 mg among current users, the relative prevalence for posterior subcapsular cataracts was 5.5 & relative prevalence for nuclear cataracts was also increased.

Source:- Cumming RG, Mitchell P, Leeder SR. Use of inhaled Corticosteroids and risk of cataracts N. Engl J.Med. 1997 July 3, 337:8-14.

Neuropsychiatric Complications in Typhoid Fever

Over a 6- year period 791 patients were studied with multidrug-resistant typhoid fever, of whom 665 individuals (84%) developed neuopsychiatric manifestations. These were: acute confusional state (73%); myelitis (6%); cerebellitis (1%); parkinsonism (1%); acute psychosis (0.6%); meningo-encephalitis (0.5%); encephalitis

(0.25%); sensory motor polyneuropathy, polymyositis, acute schizophrenia and bizarre neurological syndromes (0.12% each). Severe parkinsonian rigidity and meningo-encephalitis are associated with significant morbidity but very low mortality (0.5%).

Source:- Ali G, Samia R, Kamli M.A. ,et.al. Spectrum of neuropsychiatric complications in 791 cases of typhoid fever. Tropical Medicine and International Health 1997; Vol. 2 No. 4 pp.314-318.

Decreased Total Mortality with Postmenopausal Hormone Use

A nested case-control study of participants in the Nurses' Health Study was undertaken to determine whether postmenopausal hormone use was associated with increased total mortality.

121700 nurses (women) aged 30 to 55 years in 1976 completed questionnaires in 1976 and every 2 years until 1994. Postmenopausal women were included in the analysis. Exclusion criteria were cardiovascular disease or cancer before menopause. 3637 women died during follow-up and were considered to be the case-patients. Each women who died was matched with 10 control-women who were alive either at the date of death of diagnosis of the fatal illness (34625 control-patients). Hormone use (current, past, never) was defined according to the report on the last questionnaire completed before death, before the diagnosis of the disease that led to death, or on the questionnaire that matched the date of death for control-women. All-cause mortality and mortlity from coronary heart disease, stroke, all types of cancer, and breast cancer. The study concluded that curent use of postmenopausal hormones reduced all-cause mortality in women. The magnitude of the reduction decreased with increasing duration of use. Women with cardiovascular risk factors had the greatest benefit from use of postmenopausal hormones.

Source:- Grodstein F, Stampfer MJ, Colditz GA, et al. Postmenopausal hormone therapy and mortality. N. Engl J Med. 1997 Jun 19;336:1769-75.

Switching from Cigarettes to pipes or cigars reduced smoking-related mortality

A prospective cohort study wa undertaken by British United Provident Association (BUPA) Medical Centre, London, with a mean follow up of 14.4 years. Patients were categorized according to their smoking habits (lifelong non-smoker, former cigarette smoker who had quit>20y before study entry, pipe or cigar smoker who had never smoked cigarettes (nonswitcher), pipe or cigar smoker who had switched from cigarettes>20 . before study entry (Switcher), and current cigarette smoker). Inhaling habits (none, slight, moderate, and deep) and tobacco consumption were also assessed. Risk for death from lung cancer, ischemic heart disease, and chronic obstructive lung disease and all-cause mortality was also assessed. The study revealed that switching from cigarettes to pipes or cigars reduced the risk for death from 3 smoking-related diseases, but the risk was still greater than that in persons who had never smoked cigarettes or had never smoked at all.

Source:- Wald NJ, Watt HC. Prospective study of effect of switching from cigaettes to pipes or cigars on mortality from three smoking related diseases. BMJ. 1997 Jun 28; 314:1860-3.

A New Fertility Sparing Surgical Technique for Cervical Carcinoma

In early stage cervical carcinoma, radical hysterectomy has been the mainstay of surgical treatment. In case where fertility is to be preserved, radical tracelectomy and laparoscopic lymphadenectomy has been tried. In this paper, the authors present a new approach to preserve fertility namely abdominal radical trachelectomy. Dangent et al described a procedure called "radical trachelectomy" for exophytic tumours of stages 1a to 2a cervical carcinoma. the cervix, parametrium and upper one third of the vagina was removed with the uterus preserved and laparoscopic pelvic lymphadenectomy was done. This was a technically demanding operation. The authors tried an abdominal approach to redical trachelectomy. They say that in their technique, the ovarian vessels are not ligated and following lymphadenectomy and skeletonisation of the uterine arteries, the cervix, parametrium and vaginal cuff are excised. The residuum of the cervix is then sutured to the vagina and the uterine arteries reanastomosed. The authors conclude that their procedure may be suitable for women with early invasive cervical carcinoma who strongly desire to have children. Once they complete their animal experiments, the authors plan to perform the operation in women.

Source:- Smith JR, Boyle D.C.M., Ungar, L, etal. "Abdominal radical trachelectomy: a new surgical technique for the conservative management of cervical carcinoma"; British Journal of Obstetrics and Gynaecology; Volume 104, October 1997: 1196-1200.

DOWN MEMORY LANE

SMHS and the two Gs

G.R. Mufti MBBS, MS, M.Ch. FRCS.

Background

Going back in time...June 1995, the place... the sea resort of Brighton England, the venue for the Annual Meeting of BAUS (British Association of Urological Surgeons)... BAUS is a great meeting sparingly educational, very social and altogether a lot of fun. Like any other international meeting, while the teaching and learning chores go on, the Pharmaceutical and Instrument company barons (dare I say drug barons for short) busily entertain their established as well as potential clientele, invariably after sunset. Industrial heavyweights host big dinners where they sing the praises of their state of the art.

I was invited to such a dinner party on Wednesday the 21st of June. The audience was truly international. On my table on my right was seated Prof. Sarinder Man Singh retired Professor of Urology from AIIMS New Delhi and on my left a verbose General surgeon with a vague interest in Urology, from Sydney... a truly Australian character. After the final course I stated to look up for any acquaintances in the gathering. Three tables away from me lay a sweet surprise. There were seated Dr Muneer Khan, presently the torchbearer of Urology in Kashmir and Dr Syed Altaf who is presently working in Urology in Scotland. To find 3 Kashmiris in an assemblage of about one hundred & fifty people cheered me up, with a sense of pride. Here we were, three of us (roughly 2% of the crowd), from that beautiful part of the world (where everyone knows everyone), able to communicate to one another in the common language of Urological Surgery... (in addition to Kashmiri and half baked Hemikashmiri). Surgically speaking, come to think of it, all the three of us had one more thing in common; the surgical seed had been sown into us at one place... SMHS Hospital Srinagar, an institution unlike any other, which has served the community over generations.

Call it one of my surgical paranoia, but with my heart in my hand could I suggest that this journal has devoted statistically significant space ($P<.0001$) to the members of medical fraternity (by which I mean Physicians) of Kashmir. Well, you cannot blame the Editor for everything. It is not his fault that Gastroenterology is his occupational hazard. On a serious note we would all agree that over the years Kashmir imported and more importantly produced generations of surgeons in all disciplines with great clinical and manual skills. All these men and women along with our dear old friend SMHS deserve a space to enlighten our younger readers about these people and the great institution wherein they practised their craft. However, it is not my intention to make this a monotonous exercise of writing biographies, but to attempt to describe the whole play rather than the individual actors.

Sixties...The time for change

Many of my generation will remember the grand and majestic approach to SHMS through a beautiful tree-lined road with gardens and orchards on both sides. From the main road, it was a good ten minute drive. The sweet fruity aroma was gradually replaced by a strong antiseptic odour which heralded the arrival of the hospital, an imposing white building in the middle of nowhere. In those days, they used to employ a contingent of gardeners for the upkeep of this vast stretch of land. Whilst the world rocked to the tune of the *Beatles et al.* and its imitation the *Ina Mina Dika*, poor old SMHS felt nervous. Changes were on the horizon. The orchards and gardens were being uprooted by the builders and contractors. New buildings were being erected to accommodate the new arrivals— the

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From Medway Hospital, Kent England (Mifti)

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first batch of medical students (which included myself) who had already completed their first year in a makeshift building a mile and a half away. They would start their clinical studies on the premises in a year's time.

For SHMS, until then life had been simple. The hospital essentially comprised of four separate fiefdoms, each with varying degrees of power. Entry to the inpatient department was through an imposing gate which was manned by the strongest lads in town; their remit was to stop the massive influx of people desperate to see their near and dear ones before the official entry time of 4 p.m.. Anyone cunning, strong or rich enough to get past this battle-zone into the inpatient arena, would need a good nose coupled with some common sense to head for the desired destination. Straight on, the sign for X-Rays was unmissable. To the left lay wards 1-4 where little or no activity occurred. This was the Eye and ENT dominion governed by the pleasant and amiable Dr Harbajan Singh. To the right were wards 5-8. There was evidence of modest activity in this sector with screams of children as one approached ward 8 at the end of the corridor. This was the Empire of General Medicine (including paediatrics) controlled by two bright men known to the common Kashmiris as Alijan and Naseer.

Regal staircases led to the first on both sides. The activity was obvious. The postpartal smell of lochia assaulted the olfactory buds on the right from wards 9-14- the Obstertrics and Gynaecology Complex. This theatre of intense activity was overseen by two hardworking ladies, Drs Sawhney and Malhotra. The welcome smell of Dettol trumpeted the beginning of the General Surgical Kingdom to the left from wards 15-19/20.

The Two G's

The General Surgical Kingdom included orthopaedics and other sub specialities of surgery not to mention an occasional Abdominal Hysterectomy. Two strong well built and rather well nourished men known as Girdhari Lal and Ghulam Rasool had split this sector of SMHS equally between themselves.

I had the joy and privilege of working for both of them, mainly for Dr. G. Lal and for a brief period for Dr G. Rasool. However at the time of my qualification, the great Surgical Kingdom once ruled by two G's had been dismantled and compartmentalised by the influence and power of the new surgeons, some more aged than others, who were mainly hired hands from outside Kashmir. The two G's had wisely accepted a relative back seat in the changed world of Surgery in Kashmir. Both of them must have found it uneasy to accept working as Associate Professors (in the beginning) under a new chain of command. I guess they had no choice; come to think of it even the mighty SMHS was now being controlled by the Medical College. Yet with time they proved themselves to be as good as any imported hand in the business of surgical craft.

The times before the big change were not completely forgotten. Theatre Assistants, dressers, ward boys, compounders and Miss Sahibs (colloquial Kashmiri for nurses) narrated accounts of the past. Even both these men showed glimpses of the old from time to time. Old habits die hard! The story goes that both G's passed their Fellowship (FRCS) examination at the same time. Dr G.Rasool packed his bags quickly and made a rapid exit from England and headed straight for home probably by air, whearas Dr G. Lal feeling rather intoxicated by the success in the fellowship took his own time, collected his belongings leisurely and boarded a ship for his travel. This resulted in G. Rasool joining as a surgeon in Srinagar earlier and thus carrying a lifelong seniority over his professional competitor. Yet they had the greatest respect and admiration for each other.

As a surgeon, Dr G. Rasool was up to date, innovative and a fast operator. At times it was difficult for the assistant to keep pace with him. His gastrectomy (a relatively common operation those days) was a treat to watch. Many of his assistants will remember being his second assistant for an open cholecystectomy clutched to a Morris Retractor handle and being barraged by his left elbow and his tongue with his deep roar of 'retract'. I still remember the deep, penetrating and fixed glare of his bright eyes through his rather thick glasses. When he asked a question, it seemed that for a few moments the world had come to a standstill. Thyroid was his speciality, so much so that some people had nicknamed him Hashimoto. He knew the abdomen well. He did not believe in short cuts. According to him, surgical training had to be long and hard. The art of surgery had to be learnt from him by a process of diffusion by watching his every surgical move. He knew all his staff well and watched all his assistants closely ensuring that every surgical step taken by them met his approval. He was simple in his habits and was fit enough to cycle to work for many years before buying a car in the later years of his working life. I must admit that he looked awful on that bicycle with no back carrier. Despite his occasional volatility he was a pious gentleman with a heart of gold.

Girdhari Lal was more like Sir Launcelot Spratt of "the Doctor Series" films, a man larger than life. He always arrived with an entourage of people ahead, around and behind him, many of them waving his signature on the back of an empty Gold Flake cigarette packet (he was a heavy Gold Flake smoker and even smoked on his ward rounds), yet he had the patience to talk to each and every person, look at every wound dressing and plaster.

He could not have done this without the able assistance of his dresser the famous Akram, who was a master of 'no touch technique' in those days of sterilisation by boiling. Most of this crowd was seen to one by one in Akram's dressing room. This room was opposite and to the right of the entrance to ward 17 just outside the General Surgical Theatre. Many surgical seeds have been sown in this room. I have a number of happy and sad memories of this room. I performed my first ear lobule repair, my first circumcision and even my first vasectomy in this room. All these unwary patients who underwent these procedures in this makeshift day case theatre were either friends or relatives of Akram. At least that is what he said to us, yet we never questioned it since in that world of happy symbiosis we got an opportunity to test the surgical waters in return for a little favour to Akram by accepting his statement unreservedly. My partner in these early surgical exploits was non other than my dear friend and colleague, the late Abdul Ahad Guru who was the other House Surgeon on the firm. One day, Akram lured me into excising a rather biggish sebaceous cyst from the scalp of an unsuspecting victim under local anaethestic. Little realising that the scalp is a rather juicy area of the human body, I managed to put the last skin stitch after toiling for two and a half hours with a blood loss of at least 300 ml. In the process I lost 300 ml of my sweat. Yet G. Lal knew through Akram everything that took place in that room, since he mentioned to me the next day that he had heard that I had performed a Polya Gastrectomy in Akram's room.

G. Lal was a general surgeon to the core. He was a slow and careful operator with very strong views about principles of surgery. For instance his favourite operation for a stomach ulcer of any type was Gastrojujenostomy. He did not believe that the addition of Vagotomy made any difference to the outcome (this was a hot topic of debate those days). He could tackle anything surgical; be it orthopaedics, abdomen or neurosurgery. I saw him lift depressed fractures of the skull, perform open reduction of fractures and bone grafting and yet he could demonstrate a classical Freyer's Transvesical Prostatectomy. Open Cholecystectomy through a right paramedian incision was his favourite pastime. One day in the second theatre a newly appointed Assistant Professor who was working on a different firm was performing an Emergency Appendicectomy and was struggling to locate the appendix. G. Lal happened to wander about into this theatre after having finishing his case in his own theatre. After watching the surgeon for about five minutes, he could not resist the temptation. He took the knife in his hand and made another cut at right angles to the McBurney's incision which the young surgeon had made. The incision now looked like the letter T. The caecum, the terminal ileum, and the appendix appeared on the scene and the young Assistant Professor feeling rather embarrassed and impressed sheepishly asked Mr G as to what was the name of this T incision? G. Lal replied with a smile; "Girdhari Lal's Incision!", and walked out.

Unlike the other G he was laid back and knew only the important members of his staff. Many interns would walk through his firm for months without being noticed by him. He was awful at remembering names and even faces. He loved operating for long hours and despite looking tired and exhausted he would soldier on with his lists, sometimes well past 8 p.m.. In his later years this was violently resented by his anaesthetic colleagues, who with changing times had metamorphosed from gas men to proper doctors, which for some reason G. Lal found hard to accept. He was a generous man who loved good food and living.

It would be inappropriate and incomplete to describe the era of Drs. Ghulam Rasool and Girdhari Lal wihout mentioning the chief theatre assistant of the time called Mohamad Ismail. This gentleman was simple and amiable but very experienced and intelligent, yet he was the scorn of all the registrars and house surgeons. He would take over the charge of overall assistance during the course of an operation and make the assistants (doctors) feel defunct and unwanted. The irony was the both Gs adored him and would not undertake a major surgical step like ligating the renal artery during a Nephrectomy without quietly looking over the mask towards Mr. Ismail, who in an incomprehensible gesture signalled his seal of approval. This seemed repulsive and unacceptable to me at that time, but 30 years down the line if I analyse my surgical practice today I must admit that I do have my favourite scrub nurses as well.

The fact that I have not visited the great SMHS for over 25 years has undoubtedly helped me to write an undiluted account of Ghulam Rasool and Girdhari Lal era commonly known to many of their juniors as Lassa Bubb and Gira Kak. Their contribution to the development of surgical services in Kashmir was enormous. Their retirement truly meant the end of a generation.

DECLARATION UNDER SECTION 5 OF THE PRESS AND REGISTRATION BOOKS ACT OF 1967 AS AMENDED FROM - I (SEE RULE I)

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I Dr. G.M. Malik hereby declare that the particulars given above, are true to the best of my knowledge and belief.

Sd/-

Dr. G.M. Malik

MEET THE PROFESSOR/CONSULTANT

Name : **Ghulam Rasool Mufti**
(commonly known as Gulzar Mufti)
Date of Birth: 19-08-1944
Marital Status : Married
Permanent
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Professional Education

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M.S. (General Surgery) M.P. Shah Medical College & Irwin Group of Hospitals, Jamnagar, India. (University of Gujarat) 1969

M.Ch. (Urology) All India Institute of Medical Sciences, New Delhi, India. 1977

F.R.C.S. The Royal College of Surgeons EDINBURGH, United Kingdom. 1984.

Current Appointment:
Position Duration

Consultant Urologist to: 13-08-90- to-date
Medway Hospital,
Gillingham, Kent, (Associate University of London Teaching Hospital);
St. Bartholomew's Hospital, Rochester, Kent;
BUPA Alexandra Hospital, Walderslade, Kent;
The Somerfield Hospital Maidstone Kent.

Starting his career as a Medical Officer in a Govt. dispensary Yilgam, Kashmir in 1966 Dr. Mufti's ten years in India were utilized in acquiring superspecialization in urology. After a three year stint in Iran (1978-1981) he moved to England. Dr. Mufti has been serving as a consultant urologist to various prestgious University Hospitals in England from time to time.

Teaching Experience

Dr. Mufti has been actively involved with teaching throughout his career. He is at present on the academic staff of United Medical & Dental School of St. Thomas & Guys.

The department also has a very active academic as well as teaching programme for post graduates. They are recognised by the Royal College of Surgeons of England as the training centre for BSTs (Basic Surgical Trainees).

The Department is also recognised as the training centre for specialist registrars in Urology for accreditation as consultants.

Membership of Distinguished Organisations:

—Full Member British Association of Urological Surgeons.
—Associate Member American Urological Association.
—Honorary Member Urological Society of India.
—Honorary Life Member Association of Surgeons of India.
—Fellow of The Royal Society of Medicine London.
—Member of the working party of MRC (Medical Research Council) on Urological Cancer.
—Full Member British Endourological Society.
—Member British Prostate Group.
—Secretary British Asian Urological Sociey.

Publication:

About thirty in Indian and International journals among them, Urology, Post graduate Medical Journal, Journal Urology, British Medical Journal etc.

NEWS

- **Prof. Mohammad Sultan Khuroo** has been awarded a Fellowship of Royal College of Physicians of Edinburgh (FRCP), a fellowship of American college of Physicians of USA (FACP) and has been chosen man of year 1997 by the American Biographical Institute. Prof. Khuroo was the Director SKIMS, Soura, India and head of the Department of Gasteroenterology before he took of the job as consultant hepatologist at the prestigious King Faisal Specialist Hospital and Research Centre (KFSH).
- **The Medical Counsil of India** has decided to hold about 80 CME Programmes in India in different parts of the country, and is now in the process of preparation of the list. The Indian doctors in USA/UK and Canada are being involved to participate in the Seminars/Symposia/Workshops etc.
- **Dr. Muzaffar Ahmad** has taken over as the new Director of Health Services, J&K Govt. Srinagar.
- The New Executive body of IMA (Kashmir Branch has been elected. For membership and other details contact Dr. N.A. Mir, Gen. Secretary, P.O. Box 884, G.P.O, Srinagar.

Conference Calender

- **Eighth International Congress on Infectious Diseases, Boston MA, USA 15 - 18 May 1998** : Normal R. Stein, Ex-Director, International Society for Infectious Diseases, 181 Longwood Av. Boston, MA 02115, USA
- **VII INternational Congress on Pediatric Otorhinolaryngology, Helsinki, Finland 7-10 June 1998** : Pekka Karma, Department of Otorhinolaryngology, Helsinki University Central Hospital, Fin 00290 Helsinki, Finland.
- **XXVIII International Congress of Opthalmology, Amsterdam, The Netherlands 21-26 June 1998** : Euro-COngress Conference Management, Jan van Gourenkade 11, 1075 H P Amsterdam, The Netherlands.
- **Second International Conference on Ocular Infections, Munich, Germany 22-26 August 1998** : J. Frucht-Pery, Ocular Infections, P.O. Box 50006, Tel Aviv 61500, Israel.
- **XIth World Congresss of Gastroenterology, Vienna, Austria, September 6-11, 1998** : Secretariat, Keizersgracht 782, 1017 EC Amsterdam, The Netherlands.
- **VIII Postgraduate Course in Diabetology (Tentatively approved for 20 RSSDI Credit Hours)** : Held in March 1998 at Guwahati Medical College, Guwahati by Professor Mihir Saikia, Course Director. For Details contact: Dr. Shekhar Shah, Trincas Building, MM Road, Fancy Bazar, Guwahati 781001 Ph : (0361) 521623, 522398.
- **XXXVII Conference of National College of Chest Physicians (NACCON 98)** : Was organised by DAVV (University of Indore), Indore Chest Society and IMA Indore Branch on March 6-8, 1998 at MBM Medical College, Indore. For Details contact : Dr. Sushil Mandovra, Organising Secretary, NACCON '98, Chest & Allergy Clinic, 53, prince Yeshwant Road, (Nr Gurudwara), Indore 452004.
- **Seventh National Neurotrauma Conference will be held at Indore on 21-23 August, 1998** : For Details Please Contact : Dr. VG Dakwale, Department of Neurosurgery, Choithram Hospital, Manik Bagh Road, Indore 452001. Tel : (91) 0731-491965/65252/433410/62491-98; Fax : (91) 0731-470068, 537277.
- **Workshop on Advanced Hepatobiliary Surgery, New delhi, India 14-15 February 1998** : G.K. Pande, department of G.I. Surgery and Liver Transplantation. All India Institute of Medical Sciences, Room 1002, PC Block, New Delhi 110029, India.
- **National Update on Asthma, Indian Asthma Care Society, Jaipur, Rajasthan, India 15-16 February 1998** : Virendra Singh, C-86 Shastri Nagar, Jaipur 302016, Rajasthan, India.
- **International Conference on Reproductive Health, Mumbai, Maharashtra, India 15-19 March 1998** : Chander P. Puri, Secretary, Indian Society of Reproduction and Fertility, Institute for Research in Reproduction, Parel, Mumbai, Maharashtra 400012, India
- **Second International Meeting on Epidemiology and Prevention of Skin Disease, Bamberg, Germany 2-4 May 1998** : T.L. Diepgen, Department of Dermatology, Friedrich-Alexander-University Erlangen-Nurnberg Hartmennstr. 14, D-91052 Erlangen, Germany.
- **Third International Congress on Cutaneous Adverse Drug Reactions, Bamberg, Germany 5 May 1998** : Maja Mockenhaupt, Dokumentatioszentrum schwerer Hautreaktinen (dZh), Haupstr.7, 79104 Freiburg, Germany.

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Jaundice in Pregnancy

Jaundice occurs in about one out of every 1500 gestations, an incidence of 0.067%. Jaundice in pregnancy poses peculiar problem which may be directly related to pregnancy like fatty liver of pregnancy, familial recurrent cholestasis of pregnancy, jaundice complicating toxemia of pregnancy or HELLP syndrome (haemolysis, elevated liver enzymes, low platelets). Jaundice may be an intercurrent one affecting the pregnant women such as viral hepatitis (AE) constituting 41%, with different out come and effect on new born. Other causes may be common bile duct obstruction which occurs in 6% of patients, by stones or an underlying chronic liver disease.[1]

Acute Fatty Liver of Pregnancy

Acute fatty liver of pregnancy is a syndrome that appears in the last trimester of pregnancy or post partum characterized by jaundice, coagulopathy and central nervous system disturbances. Renal insufficiency is common, clinical and laborartory findings are nonspecific. Diagnosis is based primarily on histologic examination of liver which shows microvesicular and macrovesicular fat. Lobular architecture is usually preserved[2]. The illness has been associated with a high maternal and fetal mortality. Treatment consists of expeditious delivery and maximal supportive care which may include sodium restriction, diuretic agents, mechanical ventilation and dialysis.[3] On presentation it is often difficult to tell whether patient has pre eclampsia with HELLP syndrome or acute fatty liver. Making the differntial diagnosis is not important because treatment is same (i.e. delivery and supportive care). There are no reports of recovery from acute fatty liver prior to delivery. If patient is in labour or if the cervix is favourable and there is no evidence of fetal distress, vaginal delivery may be attempted. General anesthesia may be used if caesarean section is required however epidural or spinal anesthesia (coagulation parameters permitting) has been advocated to avoid adverse effects of general anesthesia on already compromised liver. Liver transplantation is a dramatic approach that has a limited role in management of acute fatty liver. Fetal loss of 33% has been reported[4].

Pre-eclampsia

Pre-eclampsia complicates 5% to 8% of all pregnancies. Current thinking is that it is a vascular endothelial disease that affects multiple organs including brain, heart, lung, liver, kidneys and haematological system. It has a varied presentation, for example primary involvement may be central nervous system. Other patients may present with severe liver dysfunction and intrauterine growth retardation or disseminated intravascular coagulation and acute tubular necrosis. Another may present with nephrotic range proteinuria, massive oedema and ascitis. Still another may present with pulmonary oedema.

Criteria for diagnosis of severe pre-eclampsia which usually implies the need for delivery, include the following: blood pressure >160/100mmHg, proteinuria > 5 gm/day, pulmonary oedema, urine output < 500 ml/day,, severe epigastric pain, thrombocytopenia, haemolysis, elevated liver enzymes. Strong consideration should be given to CT scan in pre-eclampsia, patients with liver dysfunction to rule out subcapsular or intra parenchymal haematoma of liver. Hepatic infarction may also occur[5]. About 50% of patients with acute fatty liver of pregnancy have the clinical features of pre-eclampsia.[6]

The standard treatment of pre-eclampsia is bed rest and delivery. Intravenous magnesium sulfate is given to prevent seizures. Anti- hypertensive drugs are usually given only to the patients who have chronic hypertension., Vaginal delivery is usually attempted in patients with pre-eclampsia. It is felt that such patients respond to oxytocin better than do non pre-eclamptic patients, however, in patients with severe pre-eclampsia at <32 weeks with an unfavourable cervix, caesarean section may be indicated.

HELLP Syndrome

Approximately 5% of patients with pre-eclampsia develop haemolysis, elevated liver enzymes and low platelets[4]. Suggested criteria for this syndrome are a lactate dehydrogenase (LDH) level >600 IU/L, AST >72 IU/L, and a platelet count <100,000/mm[7]. The management of HELLP syndrome is controversial. Many authors consider it an indication for immediate delivery because deterioration may be sudden and unpredictable.[8] Frequent misdiagnosis include gastroenteritis, cholelithiasis, idiopathic thrombocytopenic purpura (ITP), thrombotic thrombocytopenic purpura (TTP). Delivery in patients with HELLP syndrome is by the vaginal route if possible. If a caesarean section is required, it may be necessary to leave skin open and to use intraperitoneal and subfascial drains because of the coagulopathy. Packed red cells, platelets, cryoprecipitats, and fresh frozen plasma transfusion may be required. One controversy arises, in differentiating HELLP syndrome from TTP. Because the diagnosis is clinical one, with no definitive diagnostic test for either diseases, the obstetrician should consider the patient to have HELLP syndrome until proved otherwise. plasmapheresis has been used in patient with HELLP syndrome.[9]

Cholestasis of pregnancy

This type of intrahepatic cholestasis appears in last trimester of pregnancy.[1] In mild form jaundice is absent and pruritis is only abnormality. Jaundice is rarely deep. General health is preserved. There is increase of conjugated bilirubin and alkaline phosphatase, serum transaminases are normal or slightly increased. It is often familial and has been reported in mothers, sisters and daughters. The condition is benign and prognosis for mother and baby is excellent. However, there is an increased incidence of premature labour, perhaps related to bile salts crossing th placenta.[6] The condition will almost certainly return in subsequent pregnancies. Management includes cholestyramine for pruritis and intramuscular vit. K to control hypoprothrombinemia. Termination is indicated only for fetal distress.

Viral Hepatitis in Pregnancy

For the practioner and obstetrician the most important cause of jaundice is viral hepatitis. The commonest being hepatitis B and E. Both can occur as non-fulminant and fulminant hepatic failure. Most patient with hepatitis B in pregnancy are chronic asymptomatic carriers. We recommend routine screening of pregnant women for hepatitis B because the success lies in prophylaxis which can be given to infant to prevent perinatal transmission in 90% of cases. Fetal infection occurs at delivery although transplacental infection has been documented. Further more studies involving patients with hepato cellular carcinoma demonstrated a high frequency of HBSAg in their mothers, but not in their fathers. Neonates born of HBSAg positive mothers can be given active and passive immunity. Transmission by breast feeding is also possible because HBSAg is found in breast milk however this route is controversial. The benefits of breast feeding in developing countries out weighs the risks.[10]

Transmission of hepatitis A to infants from pregnant mothers with acute hepatitis does not constitute a significant problem. Immunoprophylaxis of infants born to mothers with acute hepatitis C are empiric. Immune serum globulins should be given within 24 hours of birth[10]

Hepatitis E

Hepatitis E was first described by Khuroo et al.[11] Icteric hepatitis E characteristically occurs more commonly and with great severity in pregnant ladies.[12] In fact the major cause of mortality in the epidemic disease is high rate of fulminant hepatitis in pregnant women. Data collected from out break of hepatitis E (Kashmir 1979) showed that frequency of hepatitis was greater in pregnant (17.3%) than non pregenant women (2.15%) and in men (2.8%). The frequency of disease in first, second and third trimester was 8.8%, 17.4% and 18.6% respectively. Severe disease in the form of fulminant hepatic failure developed in pregnant women (22.2%) than in non pregnant women (none of whom had fulminant hepatic failure). The over all mortality in pregnant women was found to be 20%. The reason for high mortality is not known. This high mortality has been reported from Delhi epidemic[13], Burma[14] and Khatmandu valley[15]. Hepatitis E also gets vertically transmitted.[16] The only effective positive measure remains safe pure drinking water, yet the search for vaccine is on. There is no role of immune serum globulins in preventing contact transmission of hepatitis E[17]

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Snoring: Is it a Humorous or a Pathological Condition!

Snoring, a symptom due to partial airway obstruction during sleep, may vary in severity from an occasional occurrance due to a transient problem (i.e. viral or bacterial upper respiratory Infection or Allergic rhinitis) to an every night event. It may be barely audible or mimic the sound of some machine. The main culprit for snoring is pharyngeal collapse. The airway beginning at nose traverses through the pharynx and larynx before terminating in the pulmonary alveoli. The patency of the nasal chamber, larynx and trachesbronchial tree is maintained by rigid support system whereas the pharyngeal airway, which is constituted and supported by soft tissue, maintains its patency by the dilatory action of the pharyngeal musculature coupled with the anterior displacement of the tongue by genioglossus muscle. During sleep, due to muscular relaxation and hypotonicity, the dilator effect of the pharyngeal musculature and protrussive effect of genioglossus muscle of the tongue are lost. When one sleeps in the supine position, gravity causes posterior displacement of tongue. In some people the pharynx is more complaint, predisposing them to pharyngeal collapse when they are exposed to negative inspiratory pharyngeal pressure.[1] Sleep then result in the collapse of the pharyngeal wall during inspiration causing snoring. This collapse may be partial and mild with modest noise production and no respiratory disturbance, it may be more pronounced leading to variable degree of air-way obstruction and significant systemic effect or the collapse may be complete with severe snoring punctated by apnoeic spells and severe systemic complication leading to the exaggerated form known as obstructive sleep apnoea (OSA). Alcohol and drugs like tranquillizers have been demonstrated to increase the hypotonicity of pharyngeal musculature during sleep. Nasal obstruction due to various causes also play a role in snoring.

Snoring in infants and children is usually due to adenoid and/or tonsillar hypertrophy but may also be caused by micrognathia, lingual tonsillar hypertrophy, choanal atresia or any other pathological processes that cause obstruction of the nose, pharynx or supraglottic larynx. Snoring in adults is predominantly a male characteristic and is usually seen in overweight individuals. In one study, 10% males and 5% of females snored habitually below the age of 30, whereas it was 60% in males and 40% in females in the age between 60 and 65[2].

Snoring in adults may be caused by either nasal, pharyngeal, or supraglottic laryngeal abnormality due to allergic rhinitis, adenoid and/or tonsillar hypertrophy, nasal polyps, septal deformity, laryngeal cysts and elongated redundant pharyngeal mucosa. Other causes include excessive weight causing tissues of the neck to be bulky and flacid, hypothyroidism and other gland diseases. Snoring has been implicated as a possible risk factor to hypertension, angina pectoris and heart diseases and there are several studies to demonstrate increase in frequency of these disease in the habitually snoring population[3,4,5]

Management of these patients include detailed history and thorough clinical examination including the examination or airway using Flexible Nasopharyngoscope (with the patient in recumbent position) to assess the airway patency. Lateral skiagram of the upper airway and if possible CT scan (dynamic) will help in identifying the level and degree of airway obstruction. Overnight Polysomnography will reveal the degree of OSA.

How can one reduce snoring?

Preventive measures include reduction in weight and muscle toning, avoidance of smoking, alcohol, heavy meals (4 hours before going to bed), change of posture during sleep (sleeping on side, propped up position) etc. Surgical treatment include Septoplasy, SMR, Tonsillectomy Polypectomy, Turbinoplasty, Uvulectomy and Uvuloplatophyaryngoplasty[5]. Laryngeal surgery may be carried out to remove obstructive lesion like laryngeal cyst.

Median glossectomy, Mandibular advancement and hyoid suspension are other surgical procedures resorted to when there is obstruction at the hypopharyngeal level.

Medical treatment involves use of topical or systemic decongestants, steroid and topical steroid sprays. However, the Continuous Positive Nasal Airway Pressure (CPAP) remains the mainstay of all medical treatment plan.

Snoring a malady which affects a sizable proportion of population, though carrying a significant morbidity and possible mortality, is treatable both medically and surgically. Instead of treating it as a joke as in bygone days, one should address to this problem sympathetically and an extensive evaluation and treatment of the condition initiated at the earliest.

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Hepatitis G Virus

Mohammad Sultan Khuroo, MD, DM

In 1995-96, the hepatitis G virus (HGV) was cloned and sequenced. This virus is from the group of new agents called GB viruses (GB virus A, GB virus B and GV B virus C) and is also designated as GB virus C (GBV-C). HGV is a positive-stranded RNA virus, with a genome of 10 KB and appears, on the basis of genome length and organization, to be a member of the Flaviviridae, distinct from the hepatitis C virus (HCV). HGV infection appears to be transmitted following receipt of blood from HGV RNA-positive donors. The strength of the association of HGV infection with acute hepatitis is unclear. Persons infected with the virus appear to remain persistently infected (HGV RNA-positive) for as long as nine years. Although the virus RNA can be detected with varying frequency in patients with various forms of chronic liver disease, an association of the infection with disease has not been demonstrated. The application of existing molecular techniques are likely to add at least one enterically transmitted agent and an undefined number of parenterally transmitted agents to the existing list (A to G) of hepatitis viruses. In this article, the author would like to focus on the following aspects of viral hepatitis: (1) the reasons which led to the belief that some viral hepatitis might be caused by as yet uncharacterized viruses; (2) newly characterized Flaviviruses thought to be assolciated with hepatitis, including HGV; (3) the impact of HGV virus on clinical disease; and (4) evidence that more hepatitis viruses may exist and may be cloned and sequenced in the near future.

Viral hepatitis is one of the most important global health problems, infecting hundreds of millions of individuals and responsible for more than a million deaths per year[1]. It is in the last three decades that the clinical disease and economic consequences of viral hepatitis have been recognized. During the last two decades, there has been a dramatic improvement in the understanding of viral hepatitis, the consequences of which will affect hundreds of millions of people worldwide. Up until 1995, five distinct and unrelated hepatitis viruses had been molecularly characterized (Table 1), and the clinical impact of these agents has been the focus of extensive studies. In addition to the spectrum of acute and chronic liver disease, these agents can cause a number of systemic diseases (Table 2).

Non-A-E Agents

Over the years, considerable evidence has accumulated that some forms of viral hepatitis are not etiologically related to the five known hepatitis viruses (A-E) and thus another viral agent, as yet uncharacterized, may be the cause of viral hepatitis under these situations. Also, evidence points to the existence of an as yet unknown hepatitis viral agent causing hepatitis-associated aplastic anemia (Table 3).

Table 1. Five human hepatitis virsus A-E and their clinical consequences.

Agent	Genome	Clinical consequences
Enteric		
HAV,Picornavirus,	4.5 kb, ssRNA	AH, FHF27nm
HEV, calcivirus, 32 nm	7.5 kb, ssRNA (+)	AH, FHF*
Parenteral		
HBV, hepadnavirus, 42nm	3.2kb, dsDNA	AH, FHF, CH^{+}, cirrhosis HCC
HCV, flavivirus, 30-60nm	9.4kb, ssRNA	AH, Ch^{+}, cirrhosis, HCC
HDV,satellite, 35-40 nm	1.7kb, ssRNA(-)	AH, FHF, CH**,cirrhosis, HCC

AH=acute hepatitis*; FHF=fulminant hepatic failure; CH=chronic hepatitis; HCC= hepatocellular carcinoma; *>20% in pregnant women; $^{+}$5% in adults and >90% in neonates; $^{+}$50-80%; **5% in coinfection and >50% in superinfection.

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Table - 2 Extrahepatic manifestations of hepatitis viruses.

Condition	Virus
Polyarteritis nodusa	HBV
Glomerulonephritis	HCV, HBV
Essential mixed cryoglobulinemia	HCV
Porphyria cutanea tarda	HCV
Aplastic anaemia	Non-A-E

Table-3. Clinical conditions in which novel agents may be identified and putative novel agents described in the past

Clinical condition	Pultative agent
Acute hepatitis in surgeon (GB)	GB agent
Fulminant hepatitis non A-E	Hepatitis F (toga virus)
Syncytial giant cell hepatitis	Paramyxoviridae
Non-A, non B hepatitis (non-A-E-type)	Chloroform-resistant non-tubule forming agent
Epidemic hepatitis (non-A-E-type)	None
Hepatitis-associated aplastic anemia	None

Multiple Hepatitis Episodes

Some of the earliest evidence came from clinical observations of the occurrence of multiple episodes of hepatitis in the same individual[2]. One or more than one such episode was unrelated to the existing agents (A-E) and thus pointed to a non-A-E agent (s). Such observations were commonly documented in patients receiving transfusions, intravenous drug users, hemophiliacs and dialysis patients, suggesting that the non-A-E agent may be transmitted by parenteral route. Animal transmission studies with non-A, non-B hepatitis agents was another piece of strong evidence for a non-A-E agent[3]. Chimpanzee transmission studies identified two infectious inocula, resulting in two types of disease with differences in incubation period, pattern of enzyme elevations, chronicity and ultrastructural changes (Table 4). Subsequent studies identified HCV in a chloroformsensitive, tubule-forming, infectións inoculum, and as an etiologic cause of the disease caused by this inoculum. Unresolved was the nature of the second agent and the disease caused by it (non-A-E agent).

Transfusion-Associated Hepatitis

Transfusion-associated hepatitis has, for the first time, set the stage for the existence of a non-A, non-B agent and has led to the subsequent discovery of HCV. The same clinical syndrome has set another stage for the existence of a parenterally transmitted non-A-E agent. In the multicenter Transfusion Transmitted Virus Study, it was shown that only 60% of cases originally classified as non-A, non-B hepatitis were related to HCV. Therefore, by serologic exclusion, 40% of these cases might be classified as non-A-E[4]. In the prospective study, conducted at the National Institutes of Health in Bethesda, MD, a higher proportion of cases were HCV-related, but still, 12% were classified as being of unknown etiology[5]. However, recent comparisons of incidence rates between suspected cases of non-A-E hepatitis and nontransfused or autologous transfused subjects have cast some doubt on the magnitude of transfusion-associated hepatitis of unknown etiology. In the controlled study the incidence of hepatitis C was markedly different between transfused subjects and nontransfused controls (5.4% versus 0%), whereas the incidence of non-A-E did not differ significantly among transfused and nontransfused controls (3.5% versus 3.0%). This reflected, in part, lenient criteria for defining viral hepatitis in that study, such that many nontransfused subjects met the study criteria for viral hepatitis, but probably had low-level ALT elevations related to their surgery and hospitalization rather than to viral infection[4].

Two additional studies have demonstrated low rates of transfusion-associated hepatitis of undetermined etiology, after the second-generation anti-HCV assay for donor screening has been instituted[6,7]. Though the magnitude of transfusion-associated hepatitis of undetermined etiology may be a focus of controversy, there is no doubt that this is the strongest evidence for the existence of an agent(s) other than hepatitis A-E.

Community-Acquired Hepatitis

Excellent studies at the Centers for Disease Control (CDC) have been conducted into the causation of community-acquired hepatitis[8]. The CDC has established four sentinel countries across the United States that continuously monitor acute hepatitis incidence and thus establish viral and epidemiologic cause in each case. In an analysis of 130 patients with non-A, non-B, hepatitis, 82% were determined to be HCV-related based on the determination of anti-HCV, HCVRNA and HCV antigen in the liver tissue. Thus, 18% of community-acquired hepatitis in the USA might be due to the agent(s) of non-A-E origin. A study of community-acquired hepatitis of acute non-A, non-B in Greece revealed that only 53% were HCV-related; however, PCR was not utilized to detect HCV RNA in this study. With these results in mind, 47% of community-acquired hepatitis in Greece was presumed due to an infectious agent or agents other than HCV[9]. Buti et al., in Barcelona, analyzed 341 patients presenting with acute hepatitis: 33% were due to HAV, 20% to HBV, 6% to HDV, 22% to HCV and 64 (19%) were negative for all viral markers, including HEV[10].

Thus, the pattern emerges that 20% to 50% of community-acquired hepatitis might be due to an as yet undetermined agent in Western Europe and the USA.

Studies in the Indian subcontinent have revealed HEV as the major etiologic agent for acute sporadic hepatitis. Of the 42 patients with non-A, non-B, non-C hepatitis, 27(64.2%) had acute markers of HEV, with the remaining 35% of patients classified as hepatitis non-A-E[11]

Fulminant Hepatitis

One of the most intriguing aspects of hepatitis epidemiology is defining the cause of fulminant hepatitis. In Western Europe and the USA, while some cases of fulminant hepatitis are clearly due to HAV and HBV, the majority of such cases lack markers of hepatitis A and B viruses and have been traditionally labeled as non-A, non-B hepatitis. Recent studies using anti-HCV, HCV RNA by PCR studies in sera and liver tissue have failed to incriminate HCV as an etiologic cause of fulminant hepatitis on non-A, non-B type. Overall, in five studies, samples from 81 such patients were analyzed and HCV markers were detected in only two[12-16]. These data strongly suggested that the predominant cause of fulminant hepatitis in the West is an as yet uncharacterized agent of non-A-E type. Fagan and co-workers have described toga virus-like particles in hepatectomy specimens of seven of 18 patients engrafted for acute liver failure due to non-A, non-B hepatitis[17]. The significance of these findings to the overall spectrum of fulminant hepatitis of non-A, non-B is currently unknown[18].

Chronic Hepatitis

Does a possible novel agent exist in chronic hepatitis of non-A, non-B, non-C type? Diodati and co-workers in Padua, Italy, studied 172 consecutive patients of biopsy-proven chronic hepatitis of non-A, non-B type. Overall, 156 (91%) cases were caused by HCV; thus, the remaining 9% of such cases could be caused by a novel agent[19]. Marcellin and co-workers in France studied 823 patients of histologically proven chronic hepatitis and found only 30 (3.6%) cases unrelated to HBV, HDV, HCV or autoimmune hepatitis, which were possibly related to a novel agent[20].

Syncytial Giant Cell Hepatitis

The criteria for diagnosis of syncytial giant cell hepatitis are threefold: 1) clinical features of subacute or chronic hepatitis, usually of greater than average serverity or of fulminant hepatitis; 2) biopsy findings which include fusion of hepatocytes with syncytial giant cell transformation of the liver cell cords; bridging necrosis and cholestasis being also invariably present; and 3) demonstration by electron microscopy of cytoplasmic tubular/filamentous particles that resemble nucleocapsids of Paramyxoviridae in the syncytial giant cells. Since the original description of this disease, 30 additional cases have been observed in Canada that fulfill these three criteria, and there have also been cases referred from the United States, Mexico, Europe, Australia, and Asia. Many other instances fulfill the first two criteria, but electron microscopy was not available or was not successful in demonstrating the cytoplasmic particles (candidate cases). The basic observations confirm that this is a serious disease, but there are exceptions in that some cases are not progressive, and in a few instances, response to antiviral treatment has not been successful. The identification of the putative paramyxovirus associated with these cases has proven difficult to establish and the virus is still only partially characterized. A comparison between the ultrastructural appearance of the cytoplasmic particles seen in these cases with that of known paramyxovirus is also in progress[21].

Table 4. Evidence of two types of non-A, non-B hepatitis by reinjection and cross-challenge studies in chimpanzee[3].

Infection inocula	Inoculum1	Inoculum 2
Source with	Healthy donor with ALT	Healthy donor ALT
Incubation period	2 weeks	6 weeks
Enzyme elevation	Fluctuating	Monophasic
EM change	Tubular cytoplasmic particles	Granular nuclear particles
Chronicity	High	Low
Rechallenge	Immune	Immune
Cross challenge	Disease	Disease
Chloroform treatment	Sensitive	Resistant
Agent	HCV	Non A-E

Hepatitis-Associated Anemia

The association between aplastic anemia and viral hepatitis has been well documented. In Japan, where both hepatitis and aplastic anemia are more common than in the West, hepatitis has been associated with aplastic anemia in around 8% of the patients[22]. In hepatitis-associated aplastic anemia, evaluation rarely reveals the presence of HAV and HBV, and most cases have been classified as non-A, non-B hepatitis based on serologic exclusion. Pol and co-workers compared 19 such patients to 23 patients of aplastic anemia of other or unknown etiology; anti-HCV and HCV RNA by PCR was detected in 16% and 21%, respectively, in patients with hepatitis-associated aplastic anemia, and 35% and 26% respectively in aplasia of other etiology[23].

Hibbs et al. studied 28 patients with hepatitis-associated aplastic anemia from the USA, Asia and Europe. HCV RNA was detected by PCR in 36% of patients; however, the viremia appeared to be associated with blood transfusions received after the develpment of aplastic anemia, rather than being casually related to the development of the aplastic anemia[24]. Thus, the syndrome of hepatitis-associated aplastic anemia generally cannot be attributed to HAV, HBV or HCV, strongly suggesting the existence of an additional novel agent causing the syndrome.

Waterborne Epidemic Hepatitis

Waterborne epidemics of hepatitis occur in developing countries, involving hundreds and thousands of people. The disease occurs in the adult population, with a high mortality rate in pregnant women. The illness is acute self-limiting hepatitis with no evidence of a chronic carrier state or chronic liver disease. HEV is the etiologic cause of the majority of these epidemics. Over the last few decades, since these epidemics are being regularly tested for HEV, over 30 epidemics were studied and found to be serologically related to HEV[25]. Recently, however, two epidemics of presumed waterborne disease, which lacked acute markers of HEV, have been reported in the Indian subcontinent[26]. There was no clinical or epidemiological evidence of exposure to any hepatotoxin in this population. It is strongly suspected that such epidemics were caused by another, as yet uncharacterized, agent. In the absence of any solid informatiom regarding the nature of the causative agent(s) of non-A-E hepatitis, all molecular "roads" remained open. Primate transmission studies suggested that as many as three separate non-A-E viruses might be responsible for the viral hepatitis, unrelated to known agents. In fact, application of such a molecular approach to presumed non-A-E hepatitis led to the discovery of the hepatitis G virus (HGV).

Discovery of Novel Agents

GB Agent

The first hint of a transmissible non-A-E hepatitis agent appeared over 30 years ago in the laboratory of the late Prof. F. Deinhardt. Blood serum from a surgeon (GB) induced acute hepatitis when inoculated intc tamarins (small South American monkeys). In the 1970s, the sera were tested for HAV and HBV and found to lack acute markers of either infection. In the 1980s, new assays ruled out hepatitis C and hepatitis E viruses as causative agents[1]. Thus, the GB agent held promise for identifying a novel virus. However, the true origin of the GB agent remained questionable until the recent application of modern molecular virological techniques by the virus discovery group of Abbott Laboratories in North Chicago, headed by Dr. Isa Mushahwar.

GBV-C Virus

A PCR method (representational difference analysis) was used to clone specific nucleotide sequences present in the infectious plasma of a tamarin infected with the GB hepatitis agent. Extension of sequences found in the seven original clones revealed the presence of two related but unique Flaviviral-like RNA genomes. These two newly discovered viruses were provisionally named GB virus A (GBV-A) and GB virus B (GBV-B)[27]. PCR studies indicate that GBV-A and GBV-B can be detected in tamarin serum after inoculation with the GB agent. However, GBV-B alone was found to be sufficient to cause hepatitis in the inoculated tamarins. In infected tarmarins, there was transient but specific immune response to GBV-B proteins, but no detectable immune response to GBV-A proteins[28]. GBV-A like sequences were detected in the sera of several different tamarins prior to their exposure to the GB agent. These data suggested that GBV-A may be a naturally occurring tamarin virus obtained during passage of the original GB agent in tamarins[29]. Degenerate oligonucleotide primers derived from regions highly conserved for GBV-A, GBV-B and HCV were utilized in PCR studies to determine if GBV-A and/or GBV-B could be detected in human sera. Although GBV-A and GBV-B were not found, a third novel flavilike virus was identified, provisionally named GBV-C. Additional PCR studies indicated that GBV-C is identified in the sera of several different individuals with hepatitis. The novel virus, GBV-C, was subsequently sequenced[30]

HGV

Simultaneously with these studies in the Abbott Laboratories, researchers at Genelabs Technologies Inc., Redwood City, CA, cloned and sequenced a novel virus from a patient with post-transfusion chronic hepatitis and from another person with elevated ALT and no history of hepatitis. The new virus was called hepatitis G virus (HGV). The virus was transfusion-transmissible and was associated with acute and chronic hepatitis[31]

Phylogenetics

The evolutionary relationship between the GB viruses (GBV-A, GBV-B, GBV-C), hepatitis G virus (HGV) and HCV was determined by phylogenetic analysis of the aligned viral polyprotein sequences. The data shows that none of the GB viruses possess more than 32% amino acid sequence identity with any HCV isolate. In contrast, the HCV isolates exhibit at least a 70% sequence identity with each other. The identity between GBV-A and GBV-C is 48% while that between GBV-B and GBV-A/C is below 30%. In addition, GBV-C and HGV possess 95% identity, indicating that they are independent isolates of the same virus. Thus, the novel human hepatitis virus identified is designated as hepatitis G virus (HGV) or hepatitis GB virus-C (GBV-C)[32-35].

Genomes

The genomes of GB viruses are organized like those of other flavi-and pestiviruses, with genes predicted to encode the structural and nonstructural proteins located at the '5 and 3' ends respectively (Figure 1). These viruses encode for genes for a serine protease, a helicase and an RNA-dependent RNA polymerase, consistent with other pesti-and flaviviruses. Across their entire open reading frames, the GB agents exhibit less than 27% to 48% identity to each other, suggesting that GBV-A, GBV-B and GBV-C/HGV may be classified as three new separate genera within the Flaviviridae[30-31].

Virus

HGV/GBV-C is a positive-strand RNA virus with sequence identity with various flaviviruses. The genome consists of at least 9125 nucleotides and has structural and nonstructural proteins located at the 5' and 3' ends, respectively. Sequence analysis of PCR products obtained from specimens found to contain the virus indicate that the sequences were fairly divergent (83% to 99% identical). Multiple sequence alignments demonstrated that the 5'-untranslated region (UTR) contains blocks of highly conserved sequences. The conserved deletions/insertions shifts in the reading frame resulted in the observation of three different sizes of the putative capsid protein in different isolates. Also, sequences analysis suggests that the virus encodes a single polyprotein of 2900 amino acids, which includes highly conserved motifs in NS2, NS3 and NS5. Antigen regions were identified in the putative NS3, NS4 and NS5 proteins from the virus. Epitope mapping with smaller expressed regions have identified at least four epitopes in HGV/GBV-C. Until now, five distinct genotypes of virus have been identified[30,31]

Diagnosis

GBV-C was originally identified by molecular assay utilizing degenerate oligonucleotide primers derived from the putative NS3 region of the genome and serum-derived DNA as the template. This primer pair has been used to demonstrate the presence of GBV-C sequence in case of non-A-E hepatitis, HCV sero indeterminants and intravenous drug users[30]. The second molecular assay utilized oligonucleotide primer pairs from the 5'-end sequences of GBV-C, presumably in the untranslated region of the virus. Extensive studies have been done using these primers in RT-PCR to detect GBV-C RNA in a normal blood donor, intravenous drug users and acute/chronic non-A, non-B hepatitis[34]. Automated probe-based assays have been established for the detection of GBV-C (Abbott Lex probe system). Researchers at the Genelabs, USA, have published data on HGV epidemiology using two independent primers from the NS5 region in RT-PCR to detect HGV RNA[31]. Studies at Abbott Laboratories have developed an ELISA for detection of GBV-C-specific antibodies and attempts are being made to optimize the technique[36].

Prevalence

HBV/GBV-C is detected in about 1% of volunteer blood donors with normal ALT values and in approximately 4% of blood donors with elevated ALT values. This data illustrate that the virus is present in the blood supply. It is detected in 15% of intravenous drug users, suggesting a parenteral route of transmission. HGV/GBV-C can be detected in 13% of paid plasma donors. Potentially, the virus is being transmitted through the use of contaminated blood and blood products. Approximately 20% of those individuals with acute or chronic hepatitis C virus infection are HGV/GBV-C RNA positive. The virus establishes a persistent viremia in many individuals, with viral RNA being detected for a year after infection. The virus is detected in only 7% of non-A-E hepatitis cases, including cases of fulminant hepatitis and hepatocellular carcinoma. Eighteen percent of a random population from West Africa were positive for HGV/GBV-C. This region is endemic for HBV[30,31].

Sequence of Events

Krawczynski et al. performed transmission experiments with HGV containing plasma specimens from two patients with chronic hepatitis (PNF 2161 and R 10291)[37]. Inoculation of the infectious inocula were done into chimpanzees, tamarins and cynomolgus monkeys. In chimpanzees inoculated, HGV RNA was detected in serum samples 74 to 84 days after inoculation and persisted up to 20 months after inoculation. The liver enzyme values were in the normal range throughout the observation period and no pathogenic changes were detected in liver biopsy specimens. In tamarins, liver enzyme activity was elevated beginning 30 days after inoculation and was accompanied by necroinflammatory lobular changes and portal infiltrates in the liver. Among inoculated cynomolgus monkeys, HGV RNA was detected in the serum specimen of one macaque 39 and 47 days after inoculation. These experiments provide evidence that HGV can be transmitted experimentally to nonhuman primates and cause persistent viremia. The lack of evidence of liver damage in the chimpanzee model of HGV infection may be related to the biologic characteristic of the virus replication in the liver and/or extrahepatic locations.

The natural history of HGV/GBV-C in humans was studied by Gallagher et al[38]. The authors examined serial serum samples from patients with community-acquired viral hepatitis for HGV RNA by RT-PCR. Of 12 patients evaluated, all had evidence of persistent viremia over a follow-up period extending from three to nine years. Four patterns of viremia were observed. HGV RNA persistence and titer were not associated with the presence or absence of HCV co-infection

HGV/GBV-C and Clinical Disease

HGB/GBV-C appears to be transmitted following receipt of blood from the infected donors. Persons infected with the virus appear to remain persistently infected (HGV/GBV-C RNA positive) for up to nine years. Although infection is documented in humans in many clinical situations, the strength of association of HGV/GBV-C infections with acute hepatitis and chronic liver disease is unclear and has not been fully demonstrated.

Transfusion-Associated Hepatitis

Alter et al. studied 13 cases of transfusion-associated non-A-E hepatitis from the NIH series for HGV RNA by PCR and three (23%) demonstrated the de novo appearance of the viral RNA[39]. The clinical course of these three cases was variable, one showing rapid recovery, another, delayed recovery and the third, chronic hepatitis. HGV RNA persisted in all cases for at least one year and in one case for at least four years.

Further analysis of the sera from the NIH cohort showed that the novel agent was present in 11% of 100 recipients, with minimal ALT elevations, in 10% of 62 patients with HCV-related hepatitis, nine (6%) of 152 recipients with no ALT elevations, and one (0.6%) of 157 nontransfused controls. Among HGV-RNA-positive patients, 5% met criteria of non-A-E hepatitis, 20% had minimal ALT elevations, 10% were co-infected with HCV and 65% had no biochemical evidence of liver disease. The authors concluded that HGV infection was transmitted by transfusions, caused persistent viremia and was commonly co-infected with HCV; however, the infection was commonly asymptomatic and a clear association between transfusion-associated non-A-E hepatitis and HGV could not be documented[39].

Wang et al. conducted a prospective study of transfusion-transmitted GBV-C infection in Taipei, Taiwan[40]. Among the 400 adults who had undergone cardiac surgery, 40 were positive for GBV-C RNA and seven patients were co-infected with HCV. The risk of transmission of GBV-C was estimated to be approximately 0.46% per donor. GBV-C RNA was detectable one week after transfusion and persisted for eight years with a chronicity rate of 36%. However, no evident symptoms or signs were noted in the 25 patients infected by GBV-C alone and the average peak ALT was 31 (u/L range 12-123), with persistently normal values in 20 patients. In the seven patients co-infected with HCV, the clinical course of the eight patients with transfusion-associated non-A-E hepatitis, only one was positive for GBV-C RNA. These data further strengthened the belief that this novel agent does not seem to cause clinical hepatitis in most instances[40].

Community-Acquired Viral Hepatitis

Alter et al. conducted epidemiological studies of GBV viruses on community-accquired acute viral hepatitis reported to four country healthy departments at the CDC in Atlanta, GA. An average of 17% of viral hepatitis was due to HCV and 2% were non-A-E type. GBV-A and GBV-B were detected in none of the sera; however, GBV-C RNA was detected in 20% of the HCV and 14% of the non-A-E hepatitis[41].

The clinical and demographic data of subjects infected with HGV alone, HCV alone and HCV/HGV did not differ. All HGV-infected persons had persistent viremia but none had evidence of chronic hepatitis. Chronic hepatitis developed in >60% of the HCV alone and HCV/HGV groups and in 26% of the non-A-G groups. The authors concluded that HGV accounted for only 0.3% of community-acquired acute viral hepatitis in the USA. Persistent viremia is common, but clinical disease and chronic hepatitis do not occur.

Yashima et al. studied the role of HGV infection in the etiology of acute non-A-E hepatitis from Moscow, Russia. Of the 3511 acute viral hepatitis patients studied, 40 (1.1%) lacked markers of hepatitis virsus A-E. HGV RNA wad detected in 1/28 (3%) of non-A-E patients, 9/22 (41%) of HCV patients and 0/11 (0%) of control subjects. The authors concluded that HGV was not the etiological agent of community-acquired non-A-E hepatitis in Moscow, Russia[42].

Fulminant Hepatitis

Movean et al. studied the possible role of HGV in the etiology of fulminant hepatitis of non-A-E type[43]. None of the nine such patients with fulminant hepatitis had HGV RNA detected by RT-PCR; however, two of the eight controls with HCV (n=1) and Wilson's disease (n=1) were positive for HGV RNA. Following liver transplantation, six of the nine fulminant and four of the eight controls were HGV RNA positive. The authors concluded no apparent association of HGV with non-A-E fulminant hepatitis[43]. Thomas et al. found that two of the 17 patients with fulminant non-A-E type HGV RNA positive[44].

In contrast to the above data, Riffelman et al. studied six patients with fulminant hepatitis of non-A-E type: five patients had HGV RNA detected in their acute phase sera. These data demonstrate that GBV-C was possibly associated with fulminant hepatitis of non-A-E type in Europe[45]. Similar data of association of HGV/GBV-C with fulminant hepatitis of non-A-E type have been published from Japan. Mishiro and Okamoto found GBV-C RNA in 11 out of the 22 patients with hepatitis non-A-E type in Japan[46].

Apart from the above data, preliminary data are available in which HGV/GBV-C has been investigated as an etiological agent in chronic liver disease, hepatocellular carcinoma, aplastic anemia and even thrombocytopenic purpura. The GBV-C genome was detected in around 10% of patients with chronic liver disease in Japan, suggesting GBV-C contribution to chronic liver disease is less significant than other known viruses. In another study from Japan, Kiyosawa et al. detected GBV-C RNA in four of the 25 patients with chronic liver disease of non-A-E type. Of four patients, one was positive for HBV DNA[47].

Mantero et al. studied GBV-C detection in severe aplastic anemia patients. Of the 12 patients with aplastic anemia, six patients (all severe type) had GBV-C RNA detected in sera. Among the six patients with positive GBV-C RNA, two had been co-infected with HCV. One child with positive GBV-C RNA had hepatitis-associated aplastic anemia syndrome. The authors concluded that there is a strong association between GBV-C and severe aplastic anemia in children[48]. Further data in this area shall be watched with great interest. Data also have been published implying a possible role of GBV-C in the onset of idiopathic thrombocytopenic purpura in asymptomatic HIV positive patients.

No data are currently available about the role of HGV/GBV-C in the causation of a number of clinical situations of acute and chronic liver disease of undetermined origin; these data shall be available in due course.

The clinical implications of GBV-C/HGV infection are as yet a matter of intense debate. Does this agent cause acute liver injury and can it lead to chronic liver disease? By including GBV-C/HGV in the family of hepatitis viruses, it is understood that it can cause acute and/or chronic liver disease. Most of the investigators feel that this appellation has been given to this agent rather prematurely (N Engl J Med 1996;334:1536-7). This agent as of today is in search for a condidate disease, and the search is on........

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Inflammatory Bowel Disease: Dilemma for New Drug Development

G. Nabi Mir. B. Sc; M. Pharm; PhD.

Introduction

Chronic diseases of unknown etiology are generally believed to have a multifactorial etiology leading to intricate pathogenic mechanisms that result in complex clinical manifestations. The inevitable consequence of this situation is the incapacity of dealing successfully with these disorders. In gastroenterology, few entities translate these unfortunate circumstances as well as inflammatory bowel disease. Considering drug development research for the last 30 years, experience of active investigators, present author included, has been a relative paucity of relevent animal models as the major limitation in investigating the pathogenic mechanisms responsible for the mucosal injury observed in inflammatory bowel disease (IBD). Efforts to reproduce inflammatory bowel disease in animals go back to the early 60s, but good models of Crohn's disease or Ulcerative colitis turned out to be as difficult to obtain as answers to the questions they were supposed to address. From time to time, a new animal model raises new hopes that an ideal model is finally at hand. However, as the limitations of new model become evident, expectations are lowered to realistic levels. Multiple approaches have been used in the past, in regard to both species and induction of inflammation, generating disparate information. In spite of this, substantial progress has occurred from crude models induced by acute chemical injury; long-term models have been created by the sophisticated molecular biological manipulations of genetic engineering. Recently, animal models of inflammatory bowel disease have been critically reassessed and classified as chemically induced, polymer/microbial induced, T cell/MHC perturbation associated, and spontaneous[3]. No consensus was achieved on the best single model, and no such consensus should be reached, because each model has something distinct and useful to offer. The purpose of this article is to briefly discuss recent advances in pathophysiology of various animal models. These Models have definitely advanced and accelerated new drug development.

Chemical-Induced Colitis

Epithelial or mucosal necrosis and transient and chronic inflammation can be induced by administration of either dilute acetic acid, immune complex, Trinitrobenzens Sulphonic Acid (TNBS)[4] or indomethacin in a dose-responsive fashion, as shown in Table I.

Table 1. Features of Chemical-Induced Models

Features	Acetic Acid	Immune complex	TNBS/Ethanol	Indomethacin
Animal species	Rats, mice, guinea, pigs, rabbits	Rabbits, rats	Rats, mice, rabbits	Rats, dogs, rabbits
Area of involvement	Rectum colon	Distal colon	Distal colon	Mid colon
Time Course				
Peak	1-3 days	2-3 days	2-3 days	2-3 days
Duration	2-3 days (mice)	4 days	8 wk (rats)	7-10 days
Spontaneous relapse	No	No	No	No
Pathology				
Acute/chronic	Acute	Acute	Acute and chronic	Chronic
Distribution	Continuous	Continuous	Continuous	Discontinuous
Depth of inflammation	Mucosal to transmural	Mucosa > submucosa	Transmural	Transmural
Pathogenic mechanism	Organic acid injury	Complement activation, IL-1 production	Delayed-type hypersensitivity reation against haptenmodified tissue vs. direct	Inhibitation PGE_2 and PGI_2, epithelial injury
Bacteria or their product involved	No	No	Not for induction	Perpeutation by luminal bacteria
Cytokine/inflammatory mediator abnormalities	Increased LTB_4, PGE_2 TXB_2, histamine, platelet-activating factor	Increased PGE_2, PGI_2, TXB_2, LTB_4, LTC_4, IL-1, IL-1 receptor antagonist	Increased PGE_2, LTB_4, IL-1, IL-6, IL-3/GM-CSF	Not Studied
Reproducibility (%)	100	90	100	100

GM-CSF, granulocyte-macrophage colony-stimulating factor; Ig, immunoglobulin; Il, interleukin; LT, leukotrience; PG, prostaglandin; TX, thromboxane.
(Adopted from Elson *et al*, 1995)

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Advantages of chemical-induced injury are its low cost, ease of administration, and widespread availability. However, the nonspecific nature of the initial mucosal injury that precedes the inflammatory response make these models of questionable relevance to IBD. Nevetheless, the beneficial effect of sulfasalazine, corticosteroids, and the experimental drugs in these models and the similarity of the inflammatory mediator profile to IBD suggest that the inflammatory phase bears some resemblance to human intestinal inflammation. Thus, these easily inducible models may be useful in the initial screening of new drugs, evaluating mechanisms of mucosal healing, and determining the role of luminal factors in perpetuation of nonspecific intestinal inflammation.

Features of Polymer/Microbial-Induced Colitis

Continuous administration of 5% acid-degraded carrageenan of low molecular weight or dextran sulfate sodium (DSS) in the drinking water of rats mice and guinea pigs induces cecal inflammation within 5-7 days[12].

Intramural injection of *PG-PS*[3] polymers, the primary structural cell wall component of nearly all bacterial species induces inflammation with a *variable time* course depending on the inbred rat strains used. Lymphogranuloma venereum is a sexually transmitted infection of humans characterized by primary genital lesions, suppurative lymphadenopathy, and hemorrhagic proctitis. The proctitis may be chronic and may cause rectal strictures and fistulas. It is caused by certain strains of *Chlamydia trachomtis*, an obligate Cynomologus monkeys (*Macacca fascicularis*) by rectal inoculation of the L2 serovar of *C. trachomatis*. After the initial infection, animals develop a mild proctitis that resolves in 4-6 weeks. Brief features of these models is shown in Table 2.

T Cell-Major Histocompatiblity Complex and Spontaneous Models

Cyclosporin colitis[4] model is derived from the observation that rats reconstituted with syngeneic bone marrow cells and treated with cyclosporin develop a syndrome similar to that of graft-vs.-host disease with mononuclear infiltrates and associated tissue damage evident in multiple tissues, including the intestinal mucosa, portal tracts, and skin. Two weeks after cessation of the cyclosporin treatment mice developed diarrhea associated with mononuclear inflammation in the colon.

The human class HLA-B27[3] molecule is strongly associated with susceptibility to ankylosing spondylitis and a number of other diseases collectively known as the spondyloarthropathies. To develop a model to study HLA-B27-associated disease, transgenic rats expressing the human HLA-B27 and B_2 microgiobulin genes were produced using recombinant DNA technology. Without any further manipulation, certain transgenic rat lines develop a multiorgan disease manifested by colitis, and some features of this disease resemble human colitis.

A chronic recurrent colitis occurs spontaneously in breeding colonies of cotton-top tamarins held in temperate climates. This marmoset is a monkey native to a small geographic region of Colombia. Colitis is age related typically beginning in the mid to late second year of life. At onset, disease is noted by periodic spontaneous exacerbation of acute colitis with diarrhea and weight loss. As the animals get older, they have a high frequency of adenocarcinoma of the colon, which is a common cause of death.

A new substrain of mice was generated by a program of selective breeding of C3H/HeJ[3] mice at the Jackson Laboratory, Maine, USA, a strain that had shown a propensity to develop colitis and perianal ulceration

Table 2. Features of Polymer/Microbial-Induced Models

Features	Carrageenan	DSS	PG-PS	Lymphogranuloma venereum
Animal species	Guineapig, rabbit	Mouse, rat	Rat	Monkey
Area of involvement	Cecum, colon	Colon	Ileum, colon	Rectum
Time course	3-6 wk	7-10 days	1-2 days	1-2 wk
Duration	6-8 wk	2-3 wk	2-3 days	4-6 wk
Spontaneous relapse	No	No	No	No
Pathology				
Acute/chronic	Acute > chronic	Acute and chronic	Acute and chronic	Acute and chronic
Depth of inflammation	Mucosal	Mucosal, submucosal	Transmural	Mucosal
Pathogenic mechanisms	Epithelial injury,	Epithelial injury	Activation macrophages	Intracellular infection
Bacterial or their products involved	Yes	probable	Yes	Yes
Cytokine/inflammatory mediator abnormalities	Increased PGE2, TXB2 complement deposition	Increased PGE2, TXB2, LTB, IL-2, IL-4, IL-6	Increased PGE2, NO, IL-1, IL-6, gro, IL-1 receptor antagonist, IGF-1, IkB, activation of kinin	None described
Reproducibility (%)	95	100	95	100

IGF-1, insulin-like growth factor 1; IkB, transcription growth IkB; IL, interleukin; LT, leukotriene; PG, prostaglandin; TX, thromboxane; DSS, destran sulfate (adopted from Elson et al, 1995)

Table 3. Features of T Cell-Major Histocompatibility Complex and Spontaneous Models

Features	Cyclosporin	HLA-B27/B2m Tg	Cotton-topped tamarin	C3H/HeJBir
Animal species	Mouse	Rat	Tamarin (monkey)	Mouse
Areas of involvement	Entire colon	Entire colon	Entire colon	Right colon
Time				
Peak	2-3 wk	10-20 wk age	2-3 yr age	3-6 wk age
Duration	1-4 wk	Chronically progressive	Chronically progressive	3-4 wk
Spontaneous relapse	No	No	Yes	Yes, low frequency
Pathology				
Acute/chronic	Acute and chronic	Chronic	Chronic	Acute and chronic
Depth of inflammation	Mucosal	Mucosal	Mucosal	Mucosal
Pathogenic mechanisms	T cell mediated	Abnormal antigen	Genetic susceptbility to environmental stress	Spontaneous mutant
Bacteria or their products involved	Unknown	Yes	Unknown	Likely
Cytokine/inflammatory mediator abnormalities	Increased interferon gamma, IL-2, IL-1B TNF a, granzyme A	Increased interferon gamma, IL-1, IL-6, IL-10, TNF-a	Increased leukotriene B_4 active colitis	Increased interferon gamma, IL-2, to enteric bacterial antigen
Reproducibility (%)	100	80-100	60-70	80-100

IL, interleukin; TNF, tumor necrosis factor.
(adopted from Elson *et al*, 1995)

sporadically during the past decade despite the absence of any detectable pathogen. Selective breeding of affected mice has resulted in a new substrain, C3H/HeJBir, which regularly and spontaneously develops colitis.

Models of IBD in Mutant Mice

The development of mutant models of disease by traditional genetic breeding programs depends on chance and is very time consuming. Recombinant DNA technology[3] now allows genes of interest to either be introduced into an animal (transgene) or alternatively deleted from an animal by selective gene targeting (knockout). Breeding such genetically manipulated animals produces a mutant line with a known genetic abnormality. To determine the functions that cytokines subserve in vivo, mice with knockout mutations of various cytokine genes have been generated. Some of these mice have developed chronic IBD as they age, and these are discussed in Table 4. When several of these mutations are bred into different inbred strains of mice, the severity of disease is altered, indicating the presence of genes capable of modifying disease expression. The identity of these genes is unknown but approachable with current technology. In addition, transgenic and knockout animals with no spontaneous intestinal disease may well develop disease if challenged appropriately. Thus, application of some of the existing methods discussed for generating intestinal inflammation in experimental animals to these new molecularly determined mutants seems a potentially exciting development with great promise for profound

Table 4. Features of Models of IBD in Mutant Mice

Features	IL-2	IL-10	TCR-(X TCR-0)	CD 45 RB-SCID	Ga_{12}
Animal species	Mouse	Mouse	Mouse	Mouse	Mouse
Areas of involvement	colon distal	colon	colon	colon	colon
Time course					
Onset	6-15 wk of age	4-8 wk age	3-4 mo of age	5-8 wk	8-13 wk
Duration	10-25 wk	12 wk	3-9 mo	4 wk	28 wk
Spontaneous relapse	No	No	No	No	No
Pathology					
Acute/chronic	Acute and chronic	Chronic	Acute and chronic	chronic> acute	Chronic
Depth of inflammation	Mucosal/	Mucosal	Mucosal	Mucosal	Mucosal
Pathogenic mechanisms	Cytokine/regulatory imbalance due to lack of IL-2	Cytokine/regulatory imbalance due to lack of IL-10	Gene-targeted disruption of immune molecules	Regulatory imbalance due to transfer of CD4 T cell	Unknown;gene targeted detetion of transduction signal molecules
Bacteria or their products involved	Yes	Likely	Unknown	Yes	Unknown
Cytokine/inflammatory mediator abnormalities	Deficient IL-2	Deficient IL-10 Interferon IFN-Y, TNF-(x, IL-1, IL-6)	Not defined	Increased Il-1, IL-6, TNF-(X IFN-Y, IL-3 thymus and spleen cells	Increased IL-2, IFN-7, TNF-(X by
Reproducibility (%)	100	100		75	80

IEL, intraepithelial lymphocyte; IFN, interferon; 19, immunoglobulin; IL, interleukin; TCR, T-cell receptor; TNF, tumor necero (adopted from Elson *et al*, 1995) insights into the pathogenesis of IBD.

Discussion

The IBDs represent extremely complex disorders with multiple components. These components can be thought of as an early cluster comprising the genetic, environmental, and immune system interactions important in disease induction and perpetuation and cluster of late components comprised of nonspecific inflammatory cells, cytokines, and wound healing. The latter may represent a final common pathway regardless of how the inflammation is initiated. No model exactly reproduces these human diseases; however, these models are extremely valuable in allowing research into this complexity as evidence by the progress made to date. Models have been available for some time that allow study of the late phases of nonspecific inflammation and wound healing. New models have recently become available that allow study of the early factors, particularly the complex interplay between the genetic background, immune system, and environment that is presently poorly understood but likely to be crucial in understanding these diseases. Some of the data already obtained allow certain conclusions. Multiple models are available to study the major components involved in IBD. The use of the different models depends on the component being studied and the questions addressed. Use of these models allows questions to be addressed that are not possible in humans, but their ultimate value is a complement to studies of IBD in humans, a better understanding of which is the ultimate goal.

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Importance of Pylorus Preservation in the Surgery for Duodenal Ulcer

Ajaz A. Malik MS.; N.A. Wani, M.S, FRCS, FICS.

When medical treatment has been optimal, a persistent ulcer may be judged intractable, and sugical treatment is indicated. The determination if intractability in an individual patient should entail a consideration of the patient's suffering, the extent to which it interferes with the patient's lifestyle, and an assessment of the benefits and risks of elective surgery.

All the surgical procedures for curing peptic ulcer are aimed at reduction of gastric acid secretion. Excision of ulcer itself is not sufficient as recurrence is nearly inevitable with such procedures. The five surgical methods of treating duodenal ulcer are:-

1. Subtotal gastrectomy
2. Vagotomy
3. Antrectomy
4. Gastrojejunostomy
5. Total Gastrectomy

Except in special circumstances, operation for the average patient of duodenal ulcer include:-

1. Truncal vagotomy with a drainage procedure
2. Parietal cell vagotomy without a drainage procedure
3. Vagotomy and antrectomy
4. Subtotal Gastrectomy

There is now considerable evidence that many of the sequelae of gastric surgery which may mar otherwise good results, arise from abnormalities of gastric emptying[1]. The operation of highly selective vagotomy without a drainage procedure (H.S.V.) combines an effective attack on the acid and pepsin secreting proximal part of the stomach with an attempt to preserve the mechanisms which normally control gastric emptying. This is achieved by denervating the parietal cell mass of the stomach and preserving, in addition to the hepatic and coeliac branches of the Vagus, the parasympathetic nerve supply to the antrum of the stomach - the nerves of Latarjet. No drainage procedure is added to this procedure so that an intact and innervated antrum, pylorus and duodenum are left to regulate gastric emptying.

Jordan[2] concluded in this study that slective proxmial vagotomy is superior, even though the recurrence rate of 10% at 10 years was five times greater than with truncal vagotomy and antrectomy; the basis for this judgement is in large part the near-eradication of dumping, diarrhoea, and bilious vomiting by selective proximal vagotomy. Recent summaries[2,3,4,5] show that mortality is extremely low and that dumping and diarrhoea have been almost eliminated. There is strong evidence that recurrences are caused by technical failures and that careful attention to the complete denervation of the lower oesophagus will produce substantial improvement.[6]

An operation of chronic duodenal ulcer which preserves the pylorus and deliberately retains an innervated antrum must be examined critically on two counts:

- Recurrent ulceration
- Gasric stasis

Hmphrey and Wilkinson (1972)[8] in their study emphasized than even though H.S.V. has been performed on some patients with considerable duodenal scarring, they did not have to re-operate on any patient for gastric retention. Symptoms of gastric stasis, flatulence, and food vomiting did not occur more frequenly after H.S.V. than after vagotomy and pyloroplasty. The studies of gastric emptying were particularly reassuring as they showed that gastric emptying of both fluid and semi-fluid meals is slightly more rapid than in the preoperative patient. They also concluded that omission of a drainage procedure does not lead to gastric stasis, provided that the propulsive power of the gastric antrum is retained.

Previous reports[1] have been confirmed by the studies of gastric emptying of hypertonic glucose that a fluid meal leaves the stomach more rapidly after vagotomy and drainage than in the preoperative subject. McKelvey (1970)[1] has rightly put it that the stomach is incontinent of a fluid meal after vagotomy and pyloroplasty. This picture of uncontrolled gastric emptying is not seen after H.S.V. Also the small bowel transit time is nearer to normal after H.S.V. than after Vagotomy and pyloroplasty. Hence, preservation of the pylorus-the antropyloroduodenal segment- enables controlled emptying to occur from the stomach. The corollary of this is that the incidence of unpleasant alimentary side-effects is reduced by H.S.V; leading to an increase in the proportion of good to excellent clinical results. These findings are in agreement with the observations of Killen

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and Symbas (1962)[9] that preservation of the pylorus after partial gastrectomy is accompanied by a better pattern of gastric emptying and fewer side effects. Reviewing the literature, it seems that the more the gastro-intestinal anatomy and physiology are unnecessarily interfered with, the worse may be the side effects of surgery. H.S.V. does not give perfect results. For instance, one-third of these patients experience epigastric fullness which in some necessitates a reduction in the size of meals. However, by restricting the surgical attack to the acid - and pepsin - secreting part of the stomach only and by preserving all other parts, H.S.V. seems to achieve a cure for ulcer dyspepsia without imposing too high a price in terms of post-vagotomy symptoms[8].

The operation of H.S.V. has been widely adopted because of the minimal disturbance of gastric physiology consistent with adequate acid and pepsin reduction and healing of the ulcer. Concluding the importance of pylorus preservation in surgery for duodenal ulcer, it seems advantageous in terms of technical simplicity of the procedure and preservation of the entire gastric reserviour capacity. However, the principal disadvantage being recurrent ulceration, the recurrence rate after parietal cell vagotomy is twice as high in patients with prepyloric ulcer and most surgeons use a different operative procedure for an ulcer in this location[6].

Experience with others[10,11,12,13] has shown that highly selective vagotomy without drainage has the lowest operative mortality and morbidity and fewest postoperative side-effects and longterm sequelae, when compared with all other traditional surgical methods for duodenal ulcer disease.

The preservation of more normal physiology after proximal gastric vagotomy would be expected to give it a nutritional advantage over vagotomy and antrectomy.[14]

Proximal gastric vagotomy is certainly the least disturbing procedure, from the point of view of both the effect on the physiology of the stomach and duodenum and the ease of early postoperative care. If revision is required, the field is left open in a way that it certainly is not after gastrectomy, for example. Proximal gastric vagotomy does seem to have dealt with perennial problems of dumping and diarrhoea -there is universal agreement on this point among the different series that have been published. Inspite of anxiety about the safety of the procedure following reports of sloughing of the lesser curvature of the stomach, it would seem to be just as acceptable from this point of view as are other established procedures. Other symptoms such as bilious vomiting and epigastric fullness, although present do not seem likely to spoil the effectiveness of the procedure[15,16,17]

Proximal gastric vagotomy, therefore preserving pylorus, is a logical step in the direction of conservatism in the surgical treatment of chronic duodenal ulcer, but the development of yet another operation can only be justified if there are serious objections to more established procedures. However, important problems for future consideration will be how to identify preoperative predictors for good and bad results after highly selective vagotomy and how to separate the indications for surgical as opposed to maintenance or intermittent medical treatment. The main task in the operating theatre will be to train surgeons to perform a complete and selective denervation of the parietal cell mass.

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Acute Respiratory Tract Obstruction in Children

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Abstract: *35 cases of acute respiratory tract obstruction in pediatric age group who needed surgical intervention in the form of bronchoscopy, tracheostomy or both are reviewed here. All these patients were seen and managed at National Iranian Oil Company Hospital Omidiya Khouzestan Iran, from April 1985 to April 1998. The results obtained with a review of use of instruments is described. Most of the patients presented with foreign body inhalations, some due to allergic oedema and one case had laryngeal cyst causing respiratory tract obstruction.*

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Introduction:

Acute respiratory tract obstruction is one of the most frequent and important causes which leads the patient to the emergency rooms of the hospitals. The most frequent cause of such obstruction being foreign body inhalation. In the past the mortality rate in such cases was very high, but with the advent of modern instruments and specialized techniques the mortality rate is greatly reduced. Fiberoptic endoscopes have not much role to play in these cases especially in removal of foreign bodies, these endoscopes serve to fulfill the diagnostic purpose. Use of proper sized bronchoscopes with proper catching forceps have also reduced the incidence of thoracotomy in removal of foreign body from bronchial tree.

Material and Methods

35 cases of acute respiratory tract obstruction were seen in the department of otolaryngology of N.I.O.C. Hospital Omidiya Khouzestan Iran, who needed surgical intervention for the relief of their respiratory tract obstruction. This is a 130 beded hospital with a catchment population of 300,000, having a fully equipped otolaryngology department. All these patients were brought in the emergency room except ten patients who were referred from pediatricians either from their clinics or from the wards. The patients referred from the wards (6 in number) were kept under observation by the consulting pediatricians and they subseqently developed acute respiratory embrassement and three of them had cyanosis while they were being observed by the consulting doctors.

All the patients were in pediatric age group, the youngest being 22 days old and the eldest was of 12 years of age. The male: female ratio was 3:4. All were muslims and ethnic group was as under:-

Arabs :- 20

Persian :- 15

The cause of acute respiratory tract obstruction was as follows:-

1. Foreign bodies : 20
2. Laryngeal Oedema : 14
3. Supra laryngeal cyst : 1

Symptomatology:

The following findings were seen in these patients isolated or in combination:

(Presented in order of frequency)

1. History of foreign body inhalation.
2. Acute respiratory embarrassment.
3. Cough.
4. Wheezing.
5. Cyanosis.
6. Signs of consolidation and/or atelectasis.
7. Convulsions.

Radiography was helpful only in 57% of cases. Out of 20 cases with foreign bodies 6 cases (30%) showed either radio-opaque foreign bodies or radiographic signs of consolidation or atelectasis.

All the cases of laryngeal odema showed reduced air-way space, two cases were not subjected to radiological preoperative diagnosis because of their critical conditions as both of them were cyanosed and were having convulsions. The decision to perform tracheostomy and or bronchoscopy was made by the concerned otolarngologist in all the cases 21 cases of respiratory obstruction were subjected to bronchoscopy, out of which 20 cases were foreign bodies and one case was of laryngeal odema in whom the decannulation was difficult after tracheostomy and the patient had developed right lower zone consolidation. 14 cases of laryngeal oedema were subjected to tracheostomy as in all these cases the

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conservative treatment either in the form of i.v. steroids, local vasoconstrictor sprays and oxygen inhalation had failed to relieve the obstruction and had infact become worse during the course of observation. In all these cases of laryngeal oedema the smallest size of endotracheal tube was also tried to relieve the obstruction but could not be negotiated.

The single case of laryngeal cyst under-went aspiration of the cyst through direct laryngoscope and then at later stage when the baby was in better condition and had gained some weight, at the age of three months, the cyst was excised.

During the procedures of bronchoscopy, the tracheostomy tray was kept ready but in none of the cases the tracheostomy was required and the procedure was performed without any complications. The Karl Storz bronchoscopes with appropriate sized forceps were used. All the instruments were checked before use. General anaesthesia was used in all the cases of brochoscopies, this was done without endotracheal intubation as the anaesthesia tube was connected to the side of the bronchscopes. In tracheostomies either local anaesthesia, I.V. Ketalar or no anaesthesia was used. In all the cases strong suction was always kept at hand. All the foreign bodies were removed by forceps, (cupped, crocodile, or others). Fogarty catheter was not used in removal of foreign bodies.

The following types of foreign bodies were found in the tracheo-bronchial tree:-

1. Beads	:	7 cases (35%)
2. Watermelon and other seeds	:	7 cases (35%)
3. Tomato skin	:	1 case (5%)
4. Hair clip	:	1 case (5%)
5. Whistles (Interior plastic portion)	:	2 cases (10%)
6. Safety pin	:	1 case (5%)
7. Buttons	:	1 case (5%)

The following are some cases of particular interest in our series:-

Careless Parents

A patient of 4 years age, an Arab girl was brought to the emergency department of our hospital with the history of foreign body inhalation (a bead). She had no symptoms or signs of respiratory tract obstruction and her X-ray of neck and X-ray chest were normal. The patient was admitted and kept for observation but after four hours of the admission the patient was taken home by her parents against medical advice, after saying to the incharge nurse that her foreign body has come out or she has swallowed it. Ten days after this episode the same patient was brought to the casuality department with the signs and symptoms of acute respiratory tract obstruction. The patient had severe wheezing, perspiration, intercostal recession and mild cyanosis. We recognised the patient but this time the parents gave the history that the patient had inhaled a fresh foreign body (Bead) about half an hour ago. Patient was shifted to the theatre after taking the X-rays which revealed a foreign body in the trachea and the patient respiring (Air-column) only through the hold in the bead.

After anaesthesia an infant sized bronchoscope was passed and the bead was seen impacted in the trachea with a lot of thick secretions around the foreign body. Obviously the foreign body was an old one, probably came up and got impacted. Thick mucous was aspirated by a strong suction and the foreign body got disimpacted and came a little bit up, formed a space around itself, a fine sharp crocodile forcep was passed slowly and the foreign body grasped between its hole and the edge and was taken out. Underneath there were a lot of thick muco-purulant secretions which were aspirated. Patient developed post-operative laryngeal oedema which was managed by I.V. hydrocortisone and the patient was discharged on third post-operative day.

After removal of the foreign body the parents of the patient were again interviewed who confessed and agreed that the foreign body was old and had not revealed the truth to avoid the administrative complications.

Extubation:

A three year old girl was referred from the pediatric department for her acute respiratory embarrassment and cynaosis. The patient was also seen by anaesthesiologist who had tried to intubate by the smallest sized endotrachealtube but had failed and by the time the patient was seen by us she was severely cyanosed and had convulsions. An emergency tracheostomy was performed on the bed in the ward and a temporary small sized tracheostomy tube was inserted and oxygen connected to the tube. During the procedure the patient got cardiac arrest and was resuscitated. Patient stabilised as soon as the trachea was opened and then the patient was shifted to the theatre and the tracheostomy tube changed to the appropriate size. This patient was given conservative treatment before she was referred to the E.N.T. department but all of this conservative treatment had failed to relieve the symptoms of the patient. The X-ray of the soft tissue of the neck revealed marked sub-glottic air-way obstruction. After third post-operative day we tried to decannulate the patient but she could not tolerate it and got respiratory distress and cyanosis, thus the size of the tube was gradually reduced but it did not help in extubation. On 7th post-operative day laryngo-tracheobronchoscopy was performed but it did not reveal any significant cause. On the same day the tube was changed and a metallic bivalved tube was used, this was intermittently closed for every one hour and kept open for every other hour till 13th post-operative day when the tube was successfully removed and there was no post decannulation complication.

Discussion

Acute respiratory tract obstruction is one of the important cause of death in children, although with the advent of the modern instruments and better medical care this mortality is greatly reduced.

The rigid ventilating bronchoscopes play a great role in removing the foreign bodies from tracheobronchial tree and fiberoptic bronchoscopes mainly have a diagnostic role. One of the complications reported in the literature is post-operative laryngeal oedema after bronchoscopy (Lockhart and Elliot)[1] but this complication may be avoided if one number smaller sized than required size bronchoscope is used for the procedure and if the procedure is performed quickly. In our series we had only one case who developed post-operative laryngeal oedema because of prolonged procedure.

Moazam et al[2,3] and Campbell et al have reported peanuts as the commonest type of foreign body in the tracheobronchial tree in the west, where as Ashoor et al[4] have described watermelon seeds as the commonest foreign bodies in Saudi Arabia. In our series the commonest foriegn body was watermelon seeds and beads (35% each), probably because of more consumption of watermelon in this hot area and beads because of muslim population that posses a chain of beads used for prayers. Mousali has also found watermelon seeds as the commonest foreign body in the tracheobronchial tree in the middle east[5]. The Fogarty catheter for removal of foreign bodies is not as useful as it has been published and we have found it of any use. The basket or the cup forceps or simple crocodile fine forceps were used especially in removal of beads.

Laryngeal oedema, mostly allergic, is managed by conservative treatment but some may land into the fatal complications. In our series some cases who were under the care of pediatric consultants were referred to us at a stage when their condition was critical, most of them were cyanosed and a few had convulsions. In some patients endotracheal intubation was also tried but failed and the severity of the obstruction had increased due to trauma. Most of such cases needed immediate tracheostomy.

In our series 14 such cases needed tracheostomy. None of them except one had post-operative complication of decannulation and this was over come by changing the tube to metallic type and the patient decannulated successfully after 10 days. One case of congenital supra-laryngeal cyst needed laryngoscopy and excision of the cyst (Cyst was aspirated on first visit to relieve the symptoms), such cases should always be kept in mind when a new born presents with symptoms of respiratory tract obstruction and performing direct laryngoscopy should not be neglected in such cases. All tracheostomised patients should be constantly and keenly observed in post-operative period. Experienced anaesthesiologist and otolaryngologist with modern instruments reduces the chances for thoracotomy.

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Role of Cryocauterization of Vidian Nerve Branches in Vasomotor Rhinitis

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Abstract: *Vasomotor rhinitis is caused by the overactivity of the parasympathetic nerve supply to the Nasal Mucosa. Various treatment modalities have been tried in the past to treat this condition with variable success. Experiences with Cryosurgery have shown encouraging results.This paper deals with our experience of Cryocauterization of Vidian Nerve branches in 282 patients of vasomotor rhinitis. The technique employed as well as the results are discussed.*

Key words: *Vasomotor Rhinitis, Parasympathetic, Nasal Mucosa, Vidian Nerve, Cryosurgery.*

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Introduction

Nose is prominent structure on the face which is constantly subjected to many insults and injuries by air pollutants, extremes of heat and cold, moisture, irritant dusts, pollen, chemicals, animal danders and mold spores etc. These insults lead to irritation of the nasal mucosa giving rise to symptoms like nasal obstruction, rhinorrhoea and sneezing. If no allergic cause is found the symptomatology is attributed to vasomotor rhinitis. It has been observed that persons subjected to tension, conflicts, anxieties, resentment of guilt, frustrations etc. are more prone to suffer from vasomotor rhinits.

Golding Wood[1,2] (1961, 1962)[1,2] described that all the phenomena of chronic vasomotor rhinitis are mediated purely by autonomic effects and relieved by para-sympathetic section. He postulated that hypothalamus reacts to a variety of stimuli like emotional, endocrinal, physical agents and reflex activity. This stimulation initiats a parasympathetic discharge from superior salivary nucleus that travel through nervus intermedius, greater superficial petrosal nerve, vidian nerve and to the sphenopalative ganglion, where the parasympathetic fibres synapse. The postganglionic secretomotor fibres from sphenopalatine pass through sphenopalatine foramen and thence to the nasal mucosa as nasal ganglion branches of sphenopalatine ganglion. This parasympathetic overactivity is localised and confined to nasal mucosa (Fig.1).

Till date most of the otolaryngologists have been disappointed with the results of various treatment modalities available for the treatment of vasomotor rhinitis like local or systemic decongestants, local steroid injection, chemical and electrical cauterization, turbinectomy etc., since all of them are non-specific and not based on any scientific principle. Golding-Wood [1,2,3,4] was the first person to treat vasomtor rhinits on scientific basis. He performed petrosal neurectomy and vidian neurectomy through transantral route in cases of vasomotor rhinitis. During a follow-up period ranging from 5-15 years, he observed complete relief of symptoms in 94% of pure vasomotor rhinitis cases. After the initial work by Gold-Wood, other workers described various other approaches to Vidian Nerve like transseptal by Minnis and Morrison (1971)[5], transantral subperiosteal by Nomura (1974)[6] and transnasal by Patel and Gaekwad (1975)[7]. But the fact remains that whether all these blind procedures resulted in sectioning the vidian nerve nasal branches during the course of dissection. Gold-Wood (1961)[1] in the article mentions about the success achieved by Malcolmson (1957) in some cases of vasomotor rhinitis is by just lifting the nasal mucosa over upper part of medial pterygoid plate. This elevation results in the avulsion of the vidian nerve branches in the region of sphenopalatine foramen.

Ozenberger (1973)[8] applied straight cryoprobe to the turbinates and obtained relief of nasal obstruction lasting for 3-4 years. In a few cases with complaints of sneezing and rhinorrhoea, he also applied a hooked probe to the sphenopalatine area and postulated that the autonomic secretomotor fibres to the nose are destroyed at least temporarily by this procedure. The postulation of Ozenberger (1973)[8] that the autonomic nerve regenerates fast is no longer valid, since Golding-wood (1973)[1] has reported in his long term results of patients being symptom- free for periods as long as 5-15 years.

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Material and Methods

282 patients clinically suspected to be suffereing from vasomotor rhinitis constituted the study. The age of the patients varied from 12 years to 57 years with the majority of the patients in the age group of 21-40 years. There was a predominance of males in our study (192). The various symptoms with which the patients presented along with the duration of symptoms are shown in Table I and Table II. After a thorough clinical history and otolaryngological examination all the patients were subjected to Blood examination which included Haemoglobin and Total leucocyte count. Differential leucocytic count was done to specially look for any raised eosinophil count. Nasal smears were made and stained with Toludine blue and Giemsa stain to look for any mast cells and eosinophil polymorphs etc. respectively. Table III depicts cytological picture of nasal smear. X-ray of the paranasal sinuses was done to rule out any sinus infection. Wherever sinus infection was suspected, an antral wash-out was done before cryocauterization was carried out. After history, examination and investigations the diagnosis of vasomotor rhinitis was made. The patients were subjected to cryotherapy under local anaesthesia. After premedicating the patients by giving two tablets of paracetamol (500 mg each) and one tablet of diazepam 5 mg half hour before cryoapplication, local anaesthesia was given by spraying the nasal cavities first with 4% xylocaine with 1:30,000 adrenaline and later on by placing cotton pledgets soaked in the same solution in the sphenopalatine area, ethmoidal area and floor of the nose for 10 minutes. The cryosurgical unit used in the study was devised by the author in collaboration with Asia countract Lens Laboratory Madras and works on J.T. Principle using Nitrous oxide as refrigerant. The temperature achieved was between 80°C to 85°C and the rate of cooling was 260°C per minute. the curved probe was made of silver and was having a length of 2 cm and diameter of 12 mm.

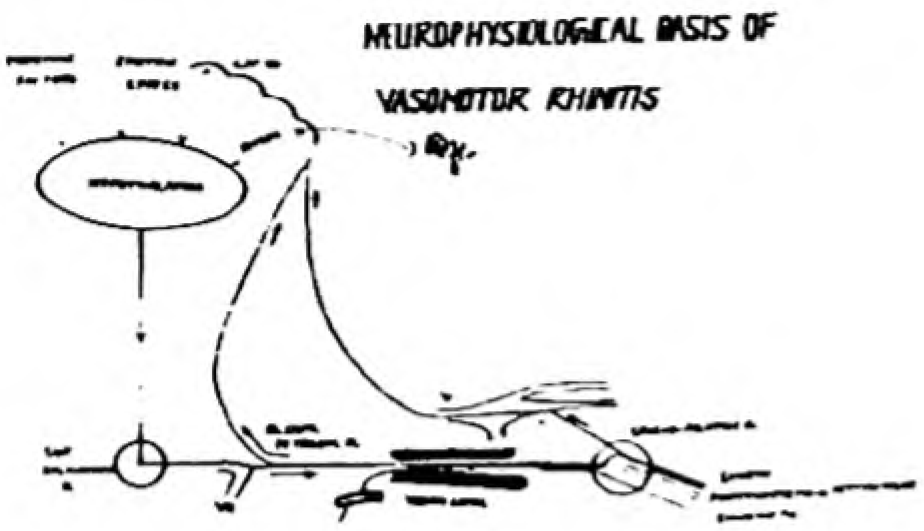


Fig. I

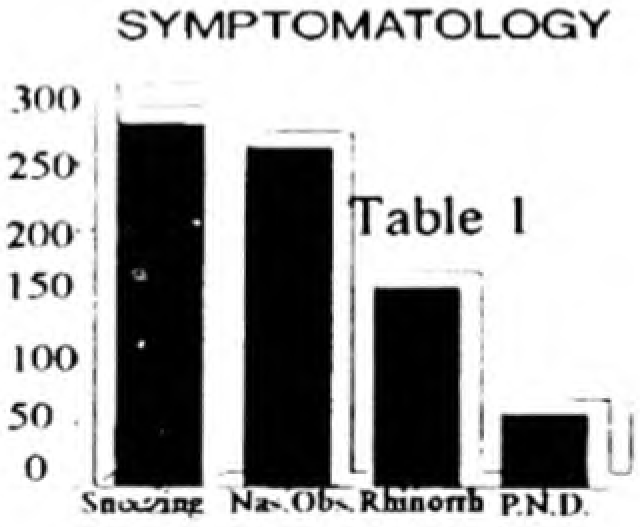
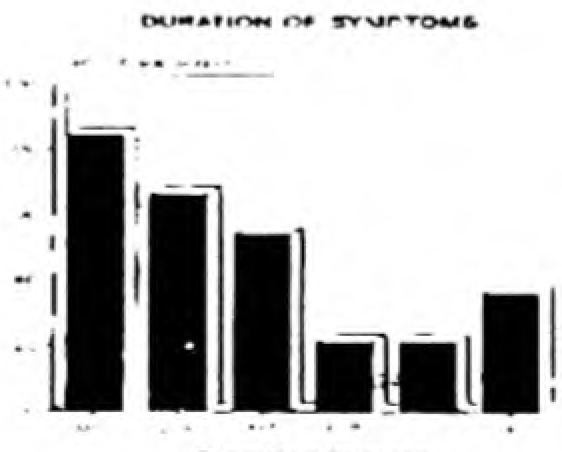


Table I



Duration in years
Table 2

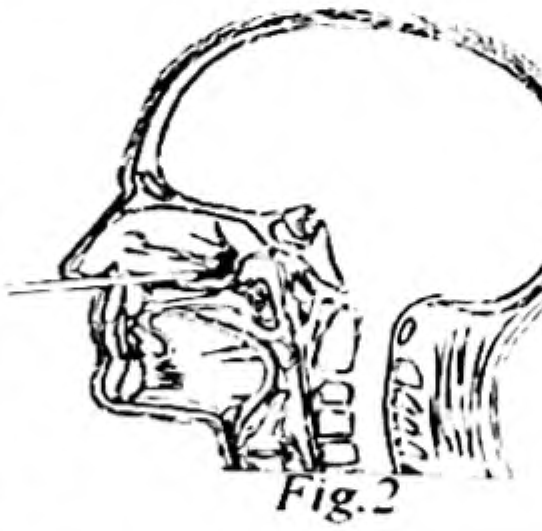


Fig.2

The patients were made to lie in semireclining position. After removing the packs, the curved cryoprobe was introduced into the nasal cavity along the side of the middle turbinate under direct vision. The posterior end of middle turbinate was hooked by the curved portion of the probe by its slight rotation laterally and freezing was started (Fig.2). The freezing countinued for two minutes. The probe was withdrawn slowly after defrosting. The exact placement of the probe and the areas frozen was confirmed by the patient's complaining of referred pain on the face supplied by the maxillary division of trigeminal nerve i.e. infraorbital region, upper jaw, infront of the ears etc during the course of freezing. The area destroyed by the curved probe is crescent shaped and measures about 10 mm x 20 mm. The patients were given antibiotics for one week and analgesics were given wherever required. The response of the treatment was evaluated on the basis of subjective improvement of symptoms like sneezing, rhinorrhoea and nasal obstruction. Complete relief was taken when the patients said relief was 95%-100%, Good response when the patient said that the relief was 75% or more, Fair response when the patient said that the relief was 50% or above and Poor response when the relief was below 50%. The patients were initially followed up at weekly, two weekly and four weekly interval and later on at monthly interval.

Observation and Discussion

It was observed that there was immediate relief of symptoms like sneezing and rhinorrhoea. The slough which is formed after cyrocauterization takes 48 to 72 hours to separate. The relief in nasal obstruction is seen only after two to three weeks of treatment. At this time the airway patency was found to be increased compared to the pretreatment stage. Apart from mild bleeding in ten patients which was controlled by nasal pinching none of the other patients had any complication.

In the present study 219 patients were treated by cryosurgery using a curved Cryoprobe which was applied to sphenopalatine area and were followed up for 2 months - 48 months. All the patients complained of sneezing and 264 patients complained of nasal obstruction. Rhinorrhoea and Postnasal drip were complained of by 156 and 157 patients respectively. 94% of the patients reported relief of sneezing and 96% of the patients reported good to complete relief of nasal obstruction at the 3 month interval. All the patients reported almost fair to complete relief of rhinorrhoea.

Principato (1979)[9] used nitrous oxide cryoprobe in 350 cases of vasomotor rhinitis and observed good results in 86% of the cases. Arora et al (1980)[10] treated 48 cases of vasomotor rhinitis by hooked cryoprobe and observed relief in sneezing and obstruction in 87.1% of their cases.

Our results are similar to the findings of these groups. Golding-Wood (1973)[4] while describing his vidian neurectomy results observed that 94% of cases had complete relief of symptoms in the follow up period of 5-15 years. It was deduced from his results that the destruction is permanent and no regeneration occurs if the nerve is coagulated for a few mm in the vidian canal. With the curved probe which we used in the present study at least 10 mm of the posterior superior nasal branch of the vidian nerve is destroyed and we hope there will be no regeneration.

Comments

Although our longest follow up has been for 48 months yet this study has revealed that this simple office treatment modality is a better alternative to vidian neurectomy in which occasional complication like ophthalmoplegia occurs, which is worse than the original disease. Also loss of lacrimation is seen with this procedure. Vidian neurectomy is a highly technical procedure requiring impeccable technique and cannot be done by every ENT surgeon. The other advantages of cryosurgry are that it is a safe and simple procedure and can be done under local anaesthesia. Treatment with cryosurgery can be repeated any number of times as opposed to vidian neurectomy which is a one time procedure. No unpleasant odour of burning is observed with this treatment. Even assuming there is return of symptoms due to regeneration it would still be worth while to repeat this simple office treatment modality to other modalities like vidian neurectomy which carry higher morbidity and some amount of risk.

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Therapeutic Splenectomy and Subsequent Infection

N.A. Wani MS.; F.Q. Parray. MS; K.A.Wani. MS; S.M.Arif MS; P.A. Khan. MS.

***Abstract** : In 102 patients who had undergone splenectomy for various hematological disorders from 1982 to 1995 at Sher-i-Kashmir Institute of Medical Sciences, Srinagar; an assessment for morbidity and mortality was made. It was found that the overall morbidity encountered was 18.62%, highest for lymphoma patients i.e. 37.5% while as overall mortality was 6.86%; highest for idiopathic hypersplenism patients (20%). This study included all age groups and an effort was made to come to a conclusion about subsequent infection following splenectomy in a broader perspective. The results indicate that complication rate is very less in carefully selected patients, patients <50 years of age but greater than 17 years, patients with shorter duration of illness, patients with mild to moderate depression in pre-operative hematological paremeters, patients without any concomitant disease and patients without any severe immunological depression.Besides, good pre-operative build up by blood and blood products, supportive measures during surgery, excellent post-operative management by supportive measures and antibiotics also form the pre-requisite for splenectomy to decrease the morbidity and mortality.*

The study indicates that therapeutic splenectomy still continues to be the mainstay of management for various hematological disorders in order to offer the patients a qualitative life inspite of the risks of infection involved.

***Key words**: Splenectomy, Infection.*

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Introduction

Hayhoe and Whitby (1955) in a treatise on "splenic function" stated that "spleen can be removed with relative impunity and low mortality and is not in any way essential to life". However, the other studies provide an evidence that spleen may be essential to life and its absence, in infancy may result in serious and overwhelming infection. King and Schumaker (1952) first suggested it and the same view point was seconded by Smith and his colleagues in later years[1,2]. But certain authors like Gross (1953), Laski and MacMillan (1959) opposed the view. Hence, the controversy still exists, but definitely because of the recent developments in anaesthetic and surgical techniques and in antibiotic therapy, the operation of splenectomy is now far safer than it was a generation ago. As a result, splenectomy may appear justifiable for more often nowadays, even in neonatal period. Another reason is that in certain disorders for which splenectomy in infancy used to be carried out, medical treatment has now been developed to an extent where it may effectively replace splenectomy, at least until the later years of childhood where operation carries a less risk.

Material and Methods

102 patients underwent splenectomy between 1982 to 1995. The age ranged from 4-72 years with a mean of 32.97 years. 49 were males (48.03%) and 53 were females (51.69%). Splenectomy was performed for various hematological disorders as shown in Table 1. All routine and specialized investigations were performed pre-operatively to reach a diagnosis. The Post-operative care included supportive measures, weaning of steroids, administring antibiotics and taking blood samples for assessment of hematological paremeters for comparison with pre-operative paremeters in order to predict the outcome. Serum immunoglobulin levels were also assessed pre-operatively and post-operatively in cases where immuno-suppression was suspected (Table-1).

Results

The results were assessed in terms of various complications encountered in the intra operative or post-operative' period. The highest morbidity was encountered in patients of primary lymphoma of spleen, followed by idiopathic hypersplenism. Agewise the highest morbidity was observed in older age group (> 60 years) i.e., 60%

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Idiopathic hypersplenism:

In this group 2 developed pneumonia, developed wound infection and 1 developed pancreatitis. The overall morbidity was 26.66% quite less as compared to Little's study (66.66%)[13]. The mortality in this group was highest (20%) when compared with other groups in our study and of course quite high when compared with other studies[8,13] probably due to advanced age with multisystem diseases.

Portal hypertension with splenomegaly:

In this group 2 patients developed infection, (22.22%) (One developed wound hematoma and one develped sepsis) which is quite less when compared with others[14,15]. We lost one young female (22 years) on 3rd post-operative day secondary to a massive gastrointestinal hemorrhage, hence the mortality was 11.11%, quite higher than reported by others.[15,16]

Malignant lymphoma:

The morbidity encountered was 37.5% i.e. 3 developed complications. One patient developed gastrointestinal hemorrhage; one developed deep venous thrombosis and one developed liver failure which is almost consistent with as observed by others[13,15]. The morbidity observed in this group was highest as compared to other groups in our study. There was no mortality in this group of patients.

The morbidity and mortality for other disorders cannot be compared with other studies as they constitute a very small group in our study.

Thus, we conclude that therapeutic splenectomy can achieve desirable therapeutic results for various hematological disorders inspite of the morbidity and mortality encountered which definitely can be lessened after carefully selecting the patients for surgery which is, of course, possible only by an excellent co-operation between the hematologist and the surgeon.

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Effect of Sub Lingual Nifedipine Pre-Treatment on Intraocular Pressure Response to Succinylcholine Administration, Laryngoscopy and Endotracheal Intubation

Javed Manzoor Wani M.D.; Abdul Qayoom Lone M.D.; Farida Ashai M.D.

Abstract : *Eighty adult patients of either sex, belonging to ASA grade 1, scheduled for different elective non ophthalmic operations were selected for the study and randomly allocated to two groups of forty patients each. Group A (control) patients recieved no pre-treatment while as group B (study) patients received nifedipine 10 mg sublingually twenty minutes before induction of anaesthesia. No untoward effects like alarming hypotension were noted in the study group intraoperatively as well postoperatively. Intraocular pressure showed a highly significant fall ($p<0.001$) following sodium thiopentone administration and highly significant rise ($p<0.001$) following succinylcholine administration, laryngoscopy and endotracheal intubation in control group while as in the study group there was a highly significant fall ($p<0.001$) following sodium thiopentone and succinylcholine administration and insignificant variation after laryngoscopy and endotracheal intubation compared to the baseline values.*

Key words: *Nifedipine, Succinylcholine administration, Tracheal intubation, Intraocular Pressure response.*

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Introduction

Open ophthalmic procedures and eye injuries pose a special problem for the anaesthetist in controlling intracular pressure and preventing loss of eyeball contents. A good anaesthetic technique always plays an important role in successful outcome of such operations. Succinylcholine is most commonly used neuromuscular blocking agent to facilitate endotracheal intubation for its adventage of providing ideal conditions but it has the disadventage of transiently increasing intraocular pressure[1] which is further aggrevated by laryngoscopy and endotracheal intubation. The safety of succinylcholine use in ophthalmic anaesthesia has been questioned by a number of workers[2,3]. The main reason for rise in intraocular pressure (IOP) following succinylcholine administration is believed to be the contracture of extraocular muscles squeezing the globe[4]. In addition a definite correlation exists between IOP, systemic arterial pressure and central venous pressure[5,6]. Attempts have been made to attenuate haemodynamic changes to laryngoscopy and endotracheal intubation[7]. These include intratracheal lidocaine spray[8], nitroglycerin administration[9] and use of nifedipine[10].

The present study was aimed to evaluate the effect of nifedipine pre treatment on IOP changes following succinylcholine administration, laryngoscopy and endotracheal intubation in non ophthalmic surgical procedures.

Material and Methods

Eighty patients in the age of 20-55 years, of either sex with physical status ASA grade 1 undergoing various elective non opthalmic surgical procedures under general anaesthesia were taken up for the study. Patients with eye ailments, preexisting raised IOP, hypertention and those with difficult intubation or who coughed or strained at the time of intubation were excluded from the study. Informed consent was taken from all the patients. No premedication was given to any of the patients. Volatile inhalational anaesthetic agents and narcotics were avoided during the study period. Patients were randomly divided into two groups of forty patients each. Group A (control) patients received no pre treatment while group B (study) received nifedipine 10mg sublingually twenty minutes before induction of anaesthesia. Heart rate (beats per minute) and blood pressure (systolic/diastolic mmHg) were constantly monitored and recorded at regular intervals as a routine.

In the operating room, after establising an I/V line with 5% dextrose in water, all patients were placed supine with the operating table in the horizontal position. Baseline reading of IOP using Schiotz tonometer was taken after topical administration of 4% lidocaine to the cornea and recorded as mean of pressures on two sides.

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This served as the baseline control value and subsequent readings were compared with the same. 10 mg nifedipine was given sublingually to the study group patients and all patients were made to rest in the supine position for 20 minutes before induction of anaesthesia. Subsequently all patients were induced with sodium thiopentone 5 mg/kg body wt. followed by succinylcholine administration 2 mg/kg body wt. Patients were ventilated on mask with 66% nitrous oxide in oxygen. Endotracheal intubation was performed one minute after succinylcholine administration and ventilation was controlled with 66% nitrous oxide in oxygen. No surgical intervention was allowed during the study period. IOP was measured and recorded at the following instances:

1. Twenty minutes before induction of anaesthesia (before nifedipine pre treatment in Group B)
2. Just before induction (Twenty minutes after pre treatment in study group).
3. After induction with sodium thiopentone.
4. After succinylcholine administration as the fasciculations ceased.
5. One minute after endotracheal intubation.
6. Two minutes after endotracheal intubation.
7. Three minutes after endotracheal intubation.

The results were evaluated statistically using students T test where $p<0.001$ was taken as highly significant.

Results

Table-I Shows some group characteristics.

Talbe-I: Age, Sex and Weight Distribution.

	Group A Mean± SD	Group B Mean ± SD
Age (Yrs.)	**34.73±8.19**	**35.05±7.17**
Weight (Kgs.)	**58.76±8.19**	**59.98±6.34**
Sex (Male: Female)	**18:22**	**14.26**

Intra-ocular pressure showed a highly significant fall ($p<0.001$) after sodium thiopentone and a highly significant rise ($p<0.001$) following succinylcholine administration in group-A patients whileas in group-B patients, there was a highly significant fall ($p<0.001$) in intra-ocular pressure following sodium thiopentone as well as succinyl choline administration. However, at 1,2 and 3 minutes after laryngoscopy and intubation a highly rise ($p<0.001$) in intra-occular pressure compared to the basal control value was only seen in group-A patients (Table-II).

Table-II: Changes in the intraocular Pressure (IOP) in two groups. Values compared to the Basal control level.

Stage of recording IOP	Group A Mean±SD	P Value	Group B Mean±SD	P Value
Basal Value	16.35±2.43	......	17.04±2.90	......
Just before sodium thiopentone	16.27±2.42	>0.20	15.86±2.74	>0.05
Just after sodium thiopentone	13.66±2.51	<0.001	12.95±2.20	<0.001**
After succinylcholine	19.90±2.92	<0.001	14.60±2.04	<0.001**
1 min. after intubation	23.88±2.27	<0.001	17.08±2.57	>0.20
2 min. after intubation	21.49±2.49	<0.001	16.26±2.37	>0.10
3 min after intubation	18.86±1.82	<0.001	15.12±2.44	<0.001*

* Significant

** Highly significant

While comparing the two groups intra-ocular pressure showed a highly significant fall ($p<0.001$) in group-B patients following succinylcholine administration and 1,2 and 3 minutes endotracheal intubation (Table-III).

Table-III: Comparison of Intraocular Pressure (IOP) between two groups at different stages.

Stage of recording IOP	Group A Mean±SD	Group B Mean±SD	P Value
Basal Value	16.35±2.43	17.04±2.90	>0.20
Just before sodium thiopentone	16.27±2.24	15.86±2.74	>0.20
Just after sodium thiopentone	13.66±2.51	12.95±2.20	<0.10
After succinylcholine	19.90±2.92	14.60±2.04	<0.001**
1 min. after intubation	23.88±2.27	17.08±2.57	>0.001**
2 min. after intubation	21.49±2.49	16.26±2.37	>0.001**
3 min after intubation	18.86±1.82	15.12±2.44	<0.001**

* Significant

** Highly significant

Discussion

The relationship between IOP and muscle relaxants is of interest to the anaesthetists for both academic and clinical reasons. Succinylcholine has been demonstrated to cause dramatic increase in IOP that may result in extrusion of vitreous humour in patients with open globe[11]. The increase in intraocular pressure following succinylcholine administration is further accentuated by laryngoscopy and endotracheal intubation[12]. In addition a sudden increase in blood pressure may cause transient but acute rise in IOP until the flow dynamics can accommodate[13].

Besides, other factors known to influence IOP include hypoxia, hypercarbia, coughing, straining and the depth of anaesthesia[14].

Major advances have been made in recent years in highly specialized field of intraocular surgery. Because of the development of improved anaesthetic agents and techniques the anaesthetist can optimize conditions for such operations.

Nifedipine (dihydropyridine) a calcium channel blocker is well absorbed by oral or sublingual routes.

After sublingual administration of 10 mg of nifedipine an antihypertensive action is obvious at 20-30 minutes[15,16]. A significant decrease in the IOP has been found in nifedipine pre-treated patients before induction of anaesthesia and nifedipine further prevented the increase in IOP after succinylcholine administration, laryngoscopy and endotracheal intubation[17]. We have also observed in our study a highly significant fall ($p<0.001$) in intraocular pressure following succinylcholine administration, laryngoscopy and endotracheal intubation in nifedipine pre-treated patients as compared to the control group. Our findings are also in accordance with Sharma et al 1992[18]. The conclusions cited above clearly indicate that pre-treatment with nifedipine 10 mg sublingually 20 minutes before induction has a positive impact in attenuating intraocular pressure response to succinylcholine administration, laryngoscopy and endotracheal intubation in young and fit adults and therefore may be helpful especially under circumstances where these changes are least desired.

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Effect of Metoprolol Pre-treatment on Sodium Nitroprusside during Deliberate Hypotension for Ligation of Patent Ductus Arteriosus

Shabia Hassan, M.D.; Javed A. Zargar, M.D.; Showkat A. Gurcoo, M.D.; Mehraj-u-din, D.A.; FFARCS

Abstract: *A prospective, placebo-controlled, randomized double-blind study was undertaken to evaluate the effects of metoprolol pre-treatment on dose requirement and effects of sodium nitroprusside used for induction of deliberate hypotension in the patients of patent ductus arteriosus (PDA) ligation. 40 patients divided into two groups of 20 patients each were administered placebo or metropolol 0.5, mgs/kg orally 60 minutes before the induction of anaesthesia. The dose requirement of sodium nitroprusside in two groups was 6.68±2.40 ug/kg/min in placebo or control group and 4.98±1.46 ug/kg/min in metoprolol group, thus showing a highly significant (p<.001) reduction in dosage requirement in metoprolol pre-treated patients. The heart rate before the start of sodium nitroprusside in control group was significantly (p<.025) higher (90.90±9.11 beats/min) when compared to metoprolol group (83.20±8.72 beats/min). During the dissection and ligation of PDA the variation in heart rate between the two groups ranged from significant (p<.005) to highly significant (p<.001). The systolic arterial pressure was reduced to the desired level of 60 mmHg in both the groups. There was no rebound hypertension in either group, although the blood pressure was on higher side in control group and difference was statistically highly significant (p<.001) when compared to metoprolol group.*

Key words: *Hypotensive anaesthesia, Sodium Nitroprusside, Metoprolol, Reflex tachycardia, Patent Ductus Arteriosus*

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Introduction

Hypotensive anaesthesia is used to facilitate the safe conduct of various surgical procedures including ligation of patent ductus arteriosus[1]. In this technique the blood pressure of anaesthetized patients is deliberately and reversibly reduced to lowest safe desired levels to achieve its benefits. Sodium nitroprusside is one of the commonest drugs used for induction of deliberate hypotension[2]. It is both venous and arterial dilator thereby capable of reducing both pre and after load. It has a rapid onset of action and the effect is terminated immediately after stopping the drug infusion. Sodium nitroprusside is a strong nitric oxide donor which explains its mechanism of action. The administration of the drug is associated with reflex tachycardia, tachyphylaxis, possible cyanide toxicity and rebound hypertension after stopping the drug[3]. Various adjuvants have been used to affect the reflex tachycardia thereby reducing the dose of sodium nitroprusside required and enhancing its hypotensive effect.

Metoprolol is a cardioselective beta adrenergic blocker. It reduces plasma renin activity in hypertensive as well as in normal patients in response to stress[4].

The present study was conducted to evalute the effects of metoprolol pre-treatment on sodium nitroprusside in patients undergoing ligation of patent ductus arteriosus under deliberate hypotension.

Material and Methods

This placebo controlled randomized double blind study was undertaken in 40 patients of either sex in the age group of 5 to 25 years posted for ligation of patent ductus arteriosus. Patients were randomly allocated to two groups of 20 each. One hour prior to induction of anaesthesia Metoprolol (0.5 mgs/kg) or placebo was administered orally with 15 mls of water. In operation theatre, a base line heart rate and blood pressure were recorded. Injection Buprenorphine 5ugs/kg was given to all patients immediately before induction. Patients were induced with sodium thiopentone 5 mgs/kg and endotracheal intubation was facilitated by suxamethonium 2mgs/kg. Anaesthesia was maintained with 66% nitrous oxide in oxygen and muscle relaxation achieved with vacuronium 100ug/kg body weight as a bolus dose and its subsequent top up dose were given when required. The radial artery was connulated using an appropriate sized intaarterial cannula for the purpose continous, invasive monitoring of blood pressure through a space-lab monitor. Sodium nitroprusside was prepared afresh in the concentration of 100ugs/ml (0.01%) in dextrose 5% and loaded in an

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infusion pump (Vicker's Medical). Infusion was started at the time of dissection around the ductus and the systolic arterial pressure was lowered to the level of 60mmHg during the ligation of ductus. Once the ductus was ligated sodium nitroprusside infusion was stopped slowly. Heart rate and blood pressure (systolic, diastolic and mean) were recorded at 5 minute intervals after starting sodium nitroprusside infusion. At the end the total volume and duration of sodium nitroprusside infusion used were noted and the total dose of the drug and its rate of infusion were calculated.

The results thus obtained were analyzed statistically using students 't' test.

Table I: Comparison of dosage of sodium nitroprusside required between the two groups

Dose of sodium nitroprusside required	Groups Control Mean±	 Metoprolol Mean±SD	p
Micrograms/kg/mt	6.68±2.40	4.08±1.46	<.001***

*** Highly significant

Results

The age, body weight, and sex in both the groups were comparable.

The dose of sodium nitroprusside required in control group and Metoprolol group was observed to be 6.68±2.40 ugs/kg/min and 4.08±1.46 ugs/kg/min respectively. The variation in the dosage requirement of sodium nitroprusside between the two groups was highly significant (p<.001) as shown in table I.

Table II: Comparison of mean heart rate between the two groups

	Group		
Stage	Control Mean±SD	Metoprolol Mean±SD	p
Before SNP	90.09±9.11	83.20±8.72	<0.25**
During SNP Infusion			
5 mts	93.75±9.61	84.65±9.33	<.005**
10 mts	95.75±9.32	85.50±8.99	<.005**
15 mts	96.55±8.61	86.10± 8.50	<.001***
20 mts	97.10±9.26	85.30±8.39	<.001***
At PDA ligation	97.45±9.40	81.65±7.03	<.001***
5 mts after stopping SNP infusion	89.45±8.91	78.73±6.83	<.001***

* N. Significant
** Significant
*** Highly significant

The mean heart rate in the control group and Metoprolol goup before starting sodium nitroprusside (base line) was 90.90±9.11 and 83.20±8.72 beats/min respectively and the difference between the two groups at this instance was significant. In control group, mean heart rate increased from baseline value at all instances of the study, although the rise was statistically significant (p<.05) at 20 mins. after starting SNP infusion and at the instance of ligation of the ductus. In the metoprolol group, the variation in the mean heart rate from base line was statistically insignificant at all instances.

When the mean heart rate between the two groups was compared the difference was significant (p<.005) at 5 and 10 minutes after the start of sodium nitroprusside infusion while as it was highly significant (p<.001) at 15 and 20 minutes after the start of sodium nitroprusside infusion and also at the time of ligation of ductus and at 5 minutes after stopping the sodium nitropusside infusion as shown in table II.

The variation in the systolic arterial pressure when compared between the two groups was statistically insignificant at all the instances upto the ligation of ductus although the variation was highly significant at 5 minutes after stopping sodium nitroprusside infusion as shown in table III.

Table III: Comparison of systolic blood pressure (mmHg) between the two groups

	Group		
Stage	Control Mean±SD	Metoprolol Mean±SD	p
Before SNP	110.25±9.51	100.50±5.64	<0.001***
During SNP Infusion			
5 mts	78.90±2.38	78.25±2.79	<.04*
10 mts	73.70±2.98	75.20±2.69	<.10*
15 mts	73.20±3.11	74.45±2.78	<.10*
20 mts	72.75±2.71	73.70±2.20	<.10*
At PDA ligation	71.90±2.47	72.76±2.30	<.10*
5 mts after stopping SNP infusion	111.65±10.14	100.10±5.76	<.001***

* NS
** Significant
*** Highly significant

Diastolic arterial pressure in the two groups before starting sodium nitroprusside was 73.20±7.22 and 67.25±5.75 mmHg respectively. The variation in diastolic arterial pressure at various instances of study between the two groups was statistically significant at base line, 15 minutes and 20 minutes after starting sodium nitroprusside and highly significant (p<.001) at the instance of ductus ligation as shown by table IV.

The mean arterial pressure at various instances in the two groups is shown in table V.

Discussion

Surgical ligation of the patent ductus arteriosus is one of the commonest closed cardiovasular surgical procedures being performed in day to day practice. Deliberate hypotension is required to facilitate the dissection and ligation of patent ductus arteriosus. The various methods and drugs that are used at present to achieve deliberate hypotension include controlled haemmorrhage, spinal anaesthesia, inhalational anaesthetics, intravenous drugs like sodium nitroprusside, nitroglycerine, trimethophan, pentolinium, alpha adrenergic blockers, beta adrenergic blockers, adenosine and prostaglandins[6,7,8,9,10,11,12]

Sodium nitroprusside is a popular agent for inducing hypotension. Despite its attractive pharmaco dynamics sodium nitroprusside induced deliberate hypotension is almost always associated with baroreceptor mediated reflex tachycardia and rebound hypertension. Many drugs which potentiate the hypotension of sodium nitroprusside have been used in clinical practice in order to reduce the total dose requirement of sodium nitroprusside and its possible untoward effects. Beta adrenergic blocking agents have been used more successfully as adjuvant to sodium nitroprusside[13]. Metoprolol, unlike propanolol is a cardioselective beta blocker. Kochweser et al (1979) claimed metoprolol to be hemodynamically superior to propranolol[14,15]

Table IV: Comparison of diastolic blood pressure (mmHg) between the two groups

	Group		
Stage	Control Mean±SD	Metoprolol Mean±SD	p
Before SNP	73.20±7.22	67.25±5.75	<.01**
During SNP Infusion			
5 mts	52.75±3.27	52.60±2.89	<.50*
10 mts	50.80±2.78	52.40±2.16	<.05*
15 mts	50.05±2.96	52.75±2.15	<.005**
20 mts	50.20±3.25	52.65±1.67	<.025**
At PDA ligation	50.20±2.44	53.20±1.67	<.001***
5 mts after stopping SNP infusion	75.50±8.66	70.65±6.34	<0.05*

* NS

** Significant

*** Highly significant

Our results of decreased dose requirement of sodium nitroprusside in metoprolol group were statistically highly significant and similar results about the dosage requirement of sodium nitroprusside have been observed in patients who were pretreated with metoprolol (0.5mgs/kg) orally by Muralidhar K et al (1988). The decrease in requirements of the sodium nitroprusside dosage with metoprolol pre-treatment was presumed to be due to a reduction in cardiac output which accompanies reduction in heart rate and secondly due to a decrease in plasma renin activity.

Our results showed a significant fall in mean heart rate in Metoprolol pretreated patients at 5 to 10 minutes and a highly significant fall at 15 and 20 minutes after SNP infusion and at the time when ductus was ligated. When compared with the control group our results were in accordance with the study conducted by Muralidhar K et al (1988) who also observed a lower heart rate during dissection and ligation of the ductus in Metoprolol pretreated patients.

Table V: Comparison of meanarterial pressure (mmHg) between the two groups

	Group		
Stage	Control Mean±SD	Metoprolol Mean±SD	p
Before SNP	85.55±7.19	78.30±4.92	<.001***
During SNP Infusion			
5 mts	61.70±2.47	61.20±2.24	<0.05*
10 mts	58.45±2.16	60.05±1.90	<0.025**
15 mts	57.85±2.50	60.00±1.62	<0.005**
20 mts	58.45±2.35	59.70±1.69	<0.05*
At PDA ligation	57.35±2.08	60.10±1.33	<.001***
5 mts after stopping SNP infusion	87.85±8.29	81.25±6.75	<.01*

* NS

** Significant

*** Highly significant

Discontinuation of sodium nitroprusside has been observed to lead to hypertensive response which may be harmful for the patient. The hypertension is believed to be due to the activation of renin angiotensin system. Hoshang J Khambatta (1970) in his study reported arterial hypertension which was higher than that recorded in the awake state. As the half life of plasma renin is 15 minutes, it is suggested that the persistently increased plasma renin activity is probably responsible for the increase of arterial pressure following sodium nitroprusside induced hypotension[16,17]

There was no rebound hypertension in either group in our study although the systolic pressure at 5 minutes of stopping sodium nitroprusside was statistically highly significant ($p<.001$) when the control group was compared with the metoprolol group. Our results were concomittant with the results of the study conducted by Murlidhar K et al (1988) who also observed increase in systolic blood pressure after stopping sodium nitroprusside in control group.

Thus it is concluded from our study dosage requirement of sodium nitroprusside is reduced and unwanted side effects associated with it are prevented in patients undergoing patent ductus arteriosus ligation when pretreated with metopolol (o.5mgs/kg).

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Mid Arm Circumference/Head Circumference Ratio-Parameter for Identifying Intra-Uterine Growth Retardation (IUGR)

G.M. Wani M.D.; Mushtaq Ahmad M.D.; Muzzafar Jan M.D.; Wajid Ali M.D.; Parvez Koul M.D.; Masood ul Hassan M.D.

Abstract: *Mid arm circumference (MAC)/Head circumference (HC) ratio is a very useful parameter for identifying intrauterine growth retardation (IUGR). 1000 neonates were subjected to anthropometric examination and it was found that MAC/HC ratio can be employed as a simple and reliable method for the detection of IUGR.*

Key words: *IUGR, MAC, HC, Anthropometry*

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Introduction

Intra-uterine growth retardation refers to a neonate whose birth weight falls below 10th percentile for the gestational period or is 2SD below mean. Out of twenty million babies born in India each year, seven million are low birth weight (less than 2500 gms) out of which 30-40% fall in IUGR group as compared to 5-7% in Western countries.[1]

Recognition of infants born wth birth weight disproportionate for their gestational age is becoming increasingly important as the growth retarded babies differ in neonatal morbidity and mortality and later development when compared to term and appropriately grown infants. Identification of IUGR is essential, as such babies are prone to complications like hypoglycemia, polycythemia, pulmonary haemorrhage and sepsis.

Although many neonates classified as small for gestational age have various complications yet others have an event free life. Birth weight alone cannot distinguish between the symptomatic and the asymptomatic small for date babies. The ability to differentiate the two would be of immense value in planning and executing medical and nursing care for the two groups of infants, minimising-routine blood drawing and decreasing parental anxiety.[2]

Birth weight measurement is not available in most of the home deliveries conducted in developing countries including India. MAC and HC ratio has been identified as a simple and accurate parameter to detect IUGR.[3] The present study has been designed to assess the prevalance of IUGR in Kashmir and utility of MAC and MAC/HC ratio to detect IUGR at birth in term neonates.

Materials and Methods

One thousand consecutive neonates of deliveries conducted at LD Hospital, Srinagar constituted the subjects for the study. Prior to delivery the propsective mothers were interviewed and examined for hypertension, heart disease, renal or collagen vascular disorders. Gestational age was assessed physically and by neurological criteria laid down by Singh et al (1975).[4] Neonates with hydrocephalus, meningocoele, encephalocoele, cephalhematoma, were excluded from the study. Anthropometic measurements were carried out in all the subjects with a fibre glass tape after 24 hours of birth by standard methods, (Jellife 1980). Various measurements included weight (lever type beam balance), Chest circumference, HC, MAC, and height.

The various parameters for each neonate were plotted on IUGR curve designed by Singh et al (1979).[5] Babies with birth weight 2±SD below normal were classified as IUGR and 2±SD above mean BW were classified as large for dates. Babies on the basis of weight were classified as:

1. Small for gestational age (SGA) less than 2.5 Kg.
2. Approp. for gestational age (AGA) between 2.5- 3.75 Kg.
3. Large for gestational age (LGA) more than 3.75 Kg.

The various values have been represented as mean ±SD. Statistical comparison were performed employing student's T-test for independent samples. A p value of <0.05 was considered significant.

Results

The neonates studied consisted of 518 males and 482 females. 212 (108 males) were small for gestational age, 774 were AGA and 14 LGA. Of the 212 SGA's. 164

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Table-I: Showing MAC and MAC/HC ratio in SGA, AGA and LGA babies.

Group (N)	MAC (Mean±SD)	MAC/HC	
SGA (n = 212)	8.42±0.48	(0.269± 0.22)	.0001
AGA (n=774)	9.82± 0.66	(0.306±0.072)	HS
LGA (n = 14)	11.74 ± 0.36	(0.338 ± 0.13)	compared to AGA

Table- II: Showing relationship of MAC, HC and MAC/HC ratio with severity of IUGR,

Group	N	MAC	HC	MAC/HC
AGA	774	9.82 ± 0.66	34.08 ± 0.76	0.306 ± 0.027
Mild IUGR	170	8.64 ± 0.54	33.63 ± 0.74	0.274 ± 0.018
Severe IUGR	42	7.50 ± 0.44	31.83 ± 0.46	0.238 ± 0.016

(77.35%) weighed from 2001 to 2500 gms, 36 (16.98%) less than 1500 gms. MAC ranged from 7.0 to 12.0cm with 73% having MAC between 9-11 cms and 21.8%<9 cms. Only 6% have MAC of >11 cms. The HC ranged from 33-35.9cm (mean 33.89±0.80) with 20.6% having HC<33 cms and 3.2% >36cms. Mean chest circumference was 30.28±0.88 (30-32 cms), with 20.7% having CC<30 cms and 5.3% having CC>32cms. The mean height was 48.28± 1.82 cms. Mean MAC, HC, CC and length of the babies with IUGR was 8.42 ±0.48 cms, 32.21±0.88 cms and 29.22±0.56 cms and 46.03±1.01 cm respectively. Table 1 depicts the MAC/Head circumference ratios of the three groups and table II the ratio of grades of IUGR. Patients with mild and severe IUGR had a MAC/HC ratio significantly different from those of the controls.

Discussion

Our study clearly demonstrates that MAC/HC ratio is a useful parameter to differentiate between patients with IUGR from those without? in Kashmiri neonates.

Meadow et al 1986 reported accurate identification of IUGR by employing MAC/HC ratio which was lowest in neonates with severe IUGR. Similar observations were reported earlier (Kumari Sharma).[2,8]

We conclude that MAC/HC ratio can be employed as a simple and reliable method for assessment of neonates for IUGR in the community and health care personnel involved in community based health care delivery system should be educated about its use.

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Primary Small Bowel Tumors - A Retrospective Clinico-Pathological Study

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***Abstract** : 25 patients of primary small bowel tumors were studied from 1991 to 1994, in the department of Medical Oncology, SKIMS. 14 patients were diagnosed to have lymphocytic-lymphoma, 6 patients had adenocarcinoma and 5 patients having leiomyosarcoma. The clinical symptoms preceded the diagnosis by an average of 6 months and all the patients wee histopathologically diagnosed following a laparotomy. Post-laparotomy treatment consisted of combination chemotherapy and 3 patients post-chemoherapy, received involved field radiation, following suspicion of residual disease. Overall mean survival was 40 weeks. Younger patients, resectability, earlier stage of disease and lower grade of malignancy were identified as favourable prognostic indices.*

***Key words:** Small Bowel, Tumors.*

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Introduction

The relative immunity of small bowel tumors is intriguing and engimatous, despite the fact that 3/4th of gastrointestinal tract length and 90% of mucosal absorptive surface is comprised by the small bowel. Fluid-alkalinity, rapid transit-time of the contents with decreased exposure to the carcinogens, lower bacterial population and metabolism resulting in the formation of fewer carcinogenic substances, presence of protective enzymes, like Benzpyrene, hydrolase helpful in detoxification of potential carcinogens and high concentration of immunoglobulin-A, are probable reasons for such uncommon occurrence.[1]

This study presents a retrospective clinico-pathological review of 25 patients, seen at Sher-i-Kashmir Institute of Medical Sciences, Srinagar during the period 1991-1994. All the patients were operated, and 21 patients had advanced unresectable growth and only palliative surgery was done. Postoperative treatment was based on histological-type. Age of the patient, stage of the disease, resectability and lower grade of malignancy determined the overall prognosis.

Small bowel tumors comprise approximately 1.5% of benign and malignant tumors of the gastrointestinal tract[2] and 75% of these are malignant[3]. The principal malignant tumors of small bowel, in order of descending frequency are: Adenocarcinoma (50%), Carcinoid (39%) and Leiomyosarcomas (11%)[1]. Among the various histologic subtypes, lymphocytic lymphomas predominate in reported literature[4,5]. By definition, primary small bowel lymphomas, are those presenting with GI symptoms as a result of lymphomatous involvement or of a predominate alimentary tract lesion,[6] account for about 15 of small bowel neoplasms, with ileum as commonest site of involvement[7]. Other malignant tumors sporadically reported include, Rhabdomyosarcoma, Liposarcoma, Angiosarcoma, Fibrosarcoma and neurogenic sarcomas. The present retrospective study, included patients treated at SKIMS only, analysed various clinical and pathological patterns of disease, which may contribute in improved understanding of this rare disease, in this part of globe.

Material and Methods

25 patients with small bowel tumors were treated in the Department of Medical Oncology, SKIMS, during the period 1991-1994. Evaluation of the patients included, a detailed history and physical examination, blood count, liver and renal function test, x-ray investigations, bone marrow examination and abdominal ultrasonography. Other investigations, namely abdominal CT scan (12 patients), upper GI endoscopy (16 patients) and Colonoscopy (13 patients) were also undertaken. A pre-operative diagnosis was seldom made because of inacuity and vague presentation in majority of the patients, mandating an exploratory laparotomy. Patients were staged according to the modified Mushoff Ann-Arbor classification, (Lymphocytic lymphomas)[8], Astler and Collar modified system, (Adenocarcinomas)[9] and Leiomyosarcomas were staged with American Joint

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Committee staging for Soft Tissue Sarcomas[10]. Histopathology in the lymphocytic lymphoma sub-group was based in accordance with the International Working formulation. For the purpose of analysis, a curative surgery was defined as removal of all the gross tumor including any involved regional lymph nodes and surrounding fatty tissue. Palliative surgery was defined as: biopsy alone (not performed endoscopically), exploratory laparotomy with finding of unresectable disease, surgery to by-pass the unresectable disease, intended curative surgery with postive proximal/distal margins of resection. Operative mortality was defined as all deaths within one month of surgery or death occuring during the same hospitalisation as the operative procedure, even if more than one month.

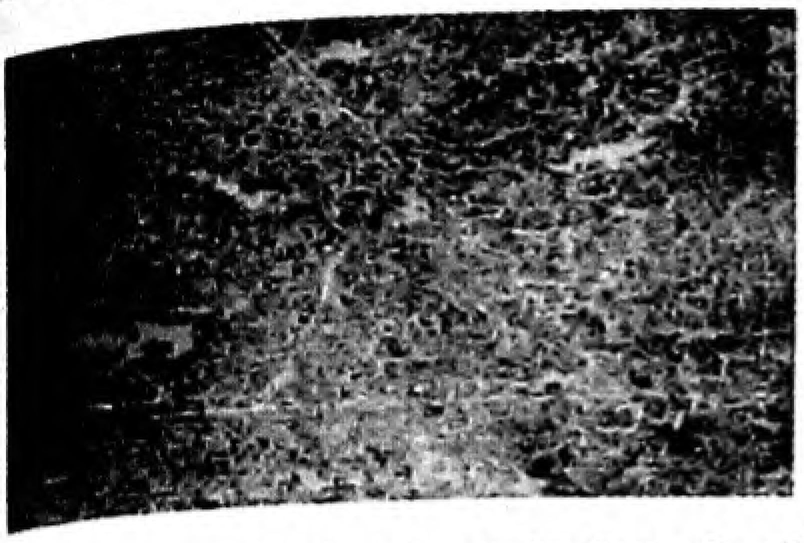
Fig.I Photomicrograph of Lymphocytic lymphoma of small bowel H&E 400

All the specimens were fixed in 8% phosphate buffered formalin, pH 7.4, embedded in paraffin and subjected to hemotoxylin and eosin, giemsa, Gomoori's reticulin, phosphotungstic acid hemotoxylin (PTAH), periodic acid schiff and Massons trichrome stain.

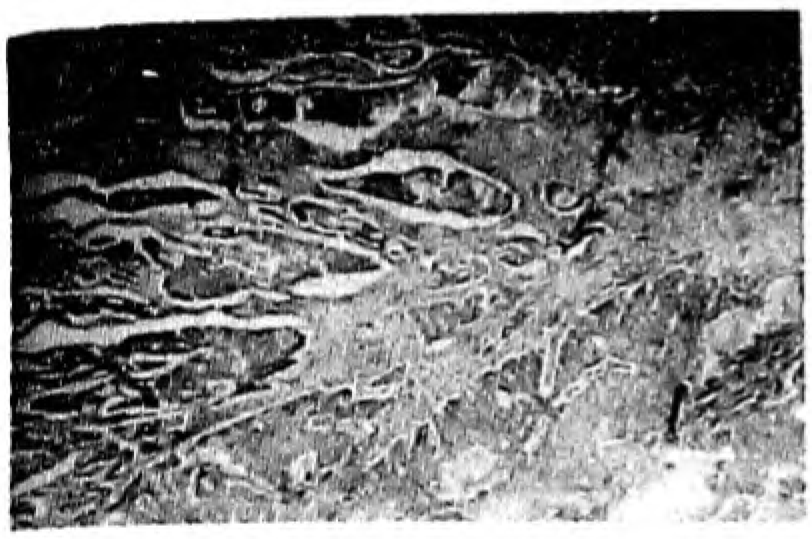
Fig. II Photomicrograph of Adenocarcinoma of small bowel H&E 400

Combination chemotherapy was used to treat patients (Table I) and patients with suspicion of resiual disease at the end of chemotherapy, were considered for radiotherapy as well. A complete response (CR) was defined as complete disappearance of all the signs and symptoms related to the tumor and recovery of normal functions. A partial response (PR) was defined as 50% reduction in the product of the longest perpendicular diameters of the measurable tumor lesions without appearance of new lesions. Stable disease was defined as less than 50% regression or improvment in symptoms accompanied by no change in tumor size for atleast 8 weeks following the start of treatment. Progressive disease was defined as continued increase in the tumor size or appearance of new lesions.

Table I: Chemotherapy protocols

Disease	Drugs	Dose	Route	q
Lymphocytic- Lymphomas	Cyclophosfamide	750mg/m^2-d1	I/V	21
	Adriamycin	50 mg/m^2-d1	I/V	
	Vincristine	1.4mg/m^2-d1	I/V	
	Predrisone	60mg/m^2-d1-5	PO	
Soft Tissue sarcomas	Hosfamide with Mesna	5gm/m^2-d1-5	CI	21
Etoposide	325mg/m^2-d1-3		I/V	
Adriamycin	50mg/m^2-d1-2		I/V	
Adenocarcinoma	5-Fluorouracil	325mg/m^2-d1,2,3,4	I/V	21
	Calcium-leucovorin 50mg		CI(4hrs)	

The representative microscopic photographs of three subgroups are illustrated in figures I, II, III.

Results

The frequency of primary small bowel tumors in our series was 0.9% of all the patients treated during 1991-94. Clinical characteristics of the patients population is summarised on table II. There were 14 patients with primary intestinal lymphoma, 6 patients had adenocarcinoma of small bowel and 5 patients had leiomyosarcoma. All the patients with lymphocytic lymphoma had tumor localised to small bowel (ileocaecal region, with 3 having extension to adjoining large gut). In adenocarcinoma sub-group, tumor was primarily localised in caecum in 1 patient and the remaining 5 patients had metastatic tumor involving liver (4 patients), lymph nodes (4 patients), iliac vesseles (2 patients), and omentum (3 patients). 4 patients in the leiomyosarcoma sub-group had tumor confined to ileum and the remaining patients had involvement of caecum and right colon.

Table II: Patient characterists

Characteristic		Number			Total
		LL	AC	LMS	
Number of patients evaluated		14	6	5	25
Sex:	Male	11	4	3	18
	Female	3	2	2	7
Age:	Median	39	50	48.6	
	Mean	40.6	47.6	48	
Clinical Profile (Overall):					
	Pain abdomen	93%		Bleeding P/R 57%	
	Mass abdomen	77%		Anorexia 50%	
	Altered bowel habits	63%		Fever, night sweats 28%	

LL= Lymphocytic lymphoma; AC = Adeonocarcinoma; LMS: Leiomyosarcoma

The depth of the invasion in case of lymphocytic lymphoma sub-group revealed invasion and extension beyond serosa in 11 patients, 2 patients upto subserosa and the remaining patients had involvement upto muscularis propria. In adenocarcinoma and leiomyo sarcoma sub-groups, all the patients had partial exoenteric tumor with extension beyond the confines of serosal sheet and involvement of adjacent viscera, vessels and nodes.

In lymphocytic lymphoma, histological subtyping was followed in accordance with Internation Working formulation, showing 11 patients having intermediate and high grade (mixed large and small cell, diffuse-2 large cell immunoblastic-9) whereas 3 patients had low grade (small cell plasmacytoid) lymphoma. In the later group, 2 patients were positive for intracytoplasmic immunoglobulin in the tumor (Ig G- L). In adenocarcinoma sub-group, histological features were consistent with an invasive, high cell grade tumor in all the patients and in the leiomyosarcoma sub-group, the tumor confines were massive, distorting the normal histology especially in the adjoining bowel, mesentery and retroperitoneum with intervening areas of ulceration and necrosis.

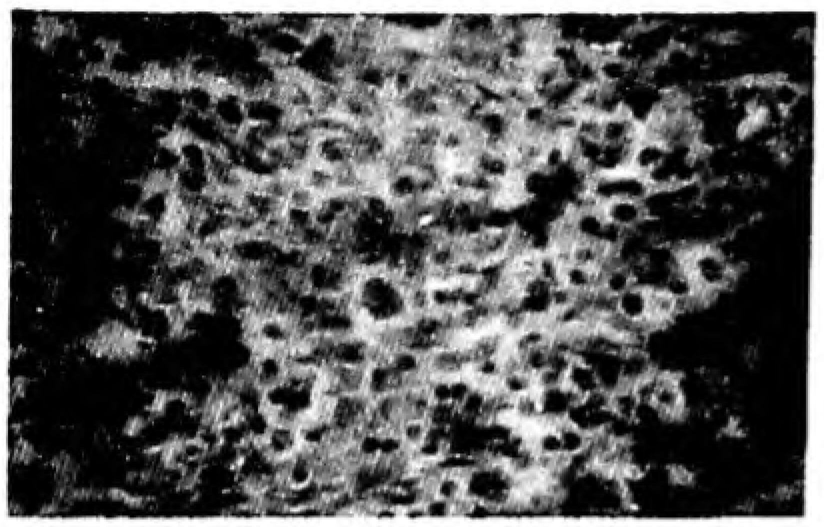

Fig.1 Photomicrograph of soft tissue sarcoma of small bowel HxB400

Histological analysis of the lymphocytic lymphoma subgroup, irrespective of the stage, revealed good prognosis of low grade lymphoma compared to those with high grade histology.

Clinical histories of patients revealed a duration of clinical symptoms before reporting to the hospital, of 6 months on an average (range 3 weeks- 15 months). Leading symptoms irrespective of disease were pain abdomen (93%), altered bowel habits (63%), anorexia (50%) and bleeding P/R (57%). None of our patients had features suggestive of malabsorption syndrome of inflammatory bowel disease.

The disease staging in 14 lymphocytic lymphoma patients was done in accordance with Mushoff and Schmidt's modification of the Ann-Arbor staging system. 6 patients (43%) had stage II_1 disease and 8 patients (57%) had stage II_2 disease. In adenocarcinoma subgroup, modified Astler-Coller system was followed, showed only one patient having Stage (C1 (T2N1) disease and remaining 5 patients (83%) had Stage C_2 (T3N1) disease. In leiomyosarcoma sub group, American Joint committee staging system was followed, showed all patients in stage IV B (G2-3T2N1M1). The treatment consisted of tumor resection in all cases, if possible, followed by multi-agent chemotherapy and/or radiation therapy. A curative surgery was done in 4 patients (3 LL, 1AC). In rest of the patients (n = 21), only palliative surgery was possible. There was no operative mortality. All the 25 patients had post-surgery chemotherapy and 3 patients had post-chemotherapy radiation treatment to the involved-field (median 25 Gy in 20 fractions) as well. The median duration of start of chemotherapy post-operatively was 34 days. In lymphocytic lymphoma, the mean number of cycles of chemotherapy received per patient were 4.6, in adenocarcinoma sub group, the mean number of cycles was 5.2 and in leiomyosarcoma subgroup, the number of cycles was 4.8.

In lymphocytic lymphoma subgroup, objective responses were noted in 7 patients (56.8%) with complete clinical remission in 5 patients (4+1 after RT) and partial remission in 2 patients. One patient had stable disease, lasting for 4 months (had received 2 cycles of chemotherapy), 6 patients (42.6%) had progression of disease and within 4-15 weeks (mean 10.8 wks) after the start of treatment. In adenocarcinoma subgroup, complete response was seen in one patient, lasting for 18 months, one patient had partial response lasting for 6 months and stable disease was noticed in 3 patients. In this subgroup, one patient was lost to follow up, after completion of 2 cycles of chemotherapy and a partial response. In leiomyosarcoma subgroup, partial response was noticed in one patient lasting for 6 months and stable disease in 4 patients lasting for an average of 15.6 weeks (range 8 wks-22 wks).

Overall, in all patients, median survival was 15 weeks (mean 40 wks). Evaluation of tumor staging in lymphocytic-lymphoma subgroup had prognostic importance. Patients with stage II_1 had better outcome than stage II_2. The 18 months disease free survival in stage II_1 was better compared to II_2. Similar results were noted in adenocarcinoma subgroup, the sole patient with C1 disease did better than C2 disease. However, in leiomyosarcoma subgroup, patients were alive and stable for a mean period of 15.6 weeks (range 8.22 wks) receiving multiagent chemotherapy .

Radical resection, irrespective of stage and disease gained a better prognosis than non-radical resection. At the end of 18 months from the start of multiagent chemotherapy and radiotherapy 5 patients in stage II_1 and 3 patients in II_2 were alive. Similarly one patient in adenocarcinoma subgroup was alive at 24 months, however, in leiomyosarcoma subgroup, no patient was alive at 18 months. Interestingly, all the patients alive at 18 months irrespective of disease and stage were aged less than 29 years, and majority of patients died at 6 months interval were more than 45 years of age. One patient in lymphocytic-lymphoma subgroup, developed adenocarcinoma of colon, while he had received 5 courses of chemotherapy (10½ months, after the diagnosis of the primary disease).

Discussion

Rare in frequency, the small bowel tumors are often misdiagnosed until a histological diagnosis is made, usually at laparotomy. The heterogeneity in the incidence and localisation of small bowel lymphomas is known[11], probably related to poor socioeconomic patterns and childhood infections. Other aetio-pathogenetic factors, viz; local (gut) immune dysregulation or chronic lymphoid stimulation with a probably malignant transformation of other disorders like pseudolymphoma, is also noted[12]. None of our patients in lymphocytic lymphoma subgroup had symptoms suggestive of inflammatory bowel disease, however, majority (more than 75%) of the patients irrespective of their disease, had monthly income less than 750/ per month. A definite and documented records of repeated childhood bowel infections was unavailable in these patients.

All patients presented with abdominal complaints, preceding the diagnosis by an average 5¼ months (range 1 mo - 20mo). The clinical profile of our patients was comparable to that of rest of studies[11], except for lowered incidence of perforation (only one patient in our series). Routine lab. investigations including hemogram, biochemistry (KFT-LFT) did not contribute to the diagnosis, however, abdominal ultrasonography done in 25/25 patients showed evidence of disease, in the form of delineation of bowel mass in lymphocytic-lymphoma and adenocarcinoma subgroups, however, the utiity of this investigation in leiomyosarcoma subgroup was restricted to mass location only besides its gross measurements. Esophago-gastroduodenoscopy in 16 patients (9/14 LL, 5/6 AC, 2/5 LMS) was normal. The endoscopic examination of colon done in 13 patients was not pathognomonic, which is in accordance with other studies as well. (Brigitte Dragosic et al).

Modified Ann-Arbor staging, classification was prognostically important in lymphocytic-lymphoma subgroup, consistent with other reports, underlying the importance of the extent of tumor spread either to regional or distant lymph nodes[11]. In adenocarcinoma subgroup, the patient with lower stage C1 fared better than advanced stage, consistent with other reports[13]. The histological features of lymphocytic-lymphoma subgroup were assessed as per working formulation, revealed a better prognosis for lower grade and intermediate grade of malignancy than high grade, which is in agreement with other results[11]. In case of adenocarcinoma subgroup, the earlier stage of disease in the sole patient revealed better survival than those with advanced disease. Interestingly, the only patient in the leiomyosarcoma subgroup, operated having some cyto-reduction, did survive with stable disease for 6 months. These observations points out the importance of the resectional surgeryof the primary tumor, even if limited, irrespective of the diagnosis, was beneficial not only to decrease the tumor burden, but also help to provide accurate staging of the disease. This is in concordance with other studies as well[14].

We are yet to encounter any recurrence of the disease 'homing phenomena' after a follow up of 24 months in patients with complete clinical remission, after initial diagnosis, however, other studies have noted, the downward trend within 2 years but can be seen as late as 14 years. One patient in the lymphocytic-lymphoma subgroup, developed adenocarcinoma (7%). This is in agreement with other reports of second malignancies complicating the treatment of lymphocytic lymphomas with multimodal treatments[15].

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Lymphadenopathy and Aspiration Cytology. (Analysis of 355 Cases of Lymph node Aspiration)

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Abstract: *In order to work out the type and frequency of different lesions in patients of lymphadenopathy in Kashmir Valley, 355 Cases reported from January to December 1995 in the Department of Pathology Govt, Medical College Srinagar were analysed. These included 226 (65.7%) cases of non-specific hyperplasia, 82 (23.7%) cases of tuberculous lymphadenitis, 15 (4.3%) cases of lymphoma and 32 (9%) cases of metastatic carcinoma in lymph node. Reactive non-specific hyperplasia of lymph node was the commonest lesion upto 40 years of age and malignancies formed 63.6 percent in the age group 41-50 years and 69 percent of all lymph-adenopathy in patients above 50 years.*

Key words: *Fine Needle Aspiration Cytology (F.N.A.C); Lympadenopathy.*

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Introduction

Lymphadenopathy is a sign of inflammation, metastatic deposits of malignant tumours or lymphoma. For the differential diagnosis of lymphodenopathy, fine needle aspiration cytology (FNAC) furnishes immediate definitive diagnosis[1] Though the first lymph node aspiration was described in 1904 by Gereig and Gray[2], it is a widely applied technique now[3]. Lymph nodes in every accessible location can be so examined. However, nodes in the head and neck areas, are by choice, the most frequent targets of aspiration biopsies[4]. FNAC of superficial lymph nodes needs to be popularised by the clinicians in view of it being a simple, safe, cheap and quick method of diagnosis.

1973 cases of aspiration cytology were reported from the Department of Pathology Govt, Medical College Srinagar (Kashmir) from January to December 1995. These included 378 Cases of lympadenopathy, out of which 23 cases had unsatisfactory smears due to insufficient cellular material and therefore no cytological diagnosis was possible. The cytological diagnosis of the remaining 355 cases of lymphadenopathy is analysed in this study. (280 enlarged lymph nodes from neck, 46 from axilla and 29 from inguinal area).

The cellular material was obtained with the help of a 20 ml, disposable syringe having 22 gauge needle. Methanol (Absolute)-fixed smears were routinely stained with May-Grunwald-Giemsa (MGG) stain. Special stains like Zieh Neelson's stain, Haematoxylin-Eosin or Papanicolaou stain were used as and when required.

The cytological diagnosis was confirmed clinically (response to therapy) or by his-to-pathology.

Results

The lesions discoved were as follows:-

1. Inflammatory, 2. lymphomas 3. and metastatic lesions (Table-I). 226 (63.7%) cases had non-specific hyperplasia of lymph nodes and 164(78%) occured in patients below 20 years and only 5(2%) cases occured in patients above 50 years of age. Cytologically, cell rich smears revealed, polymorphic lymphoid cells, predominantly small lymphocytes with few neutrophils, plasma cells, histiocytes, large tingible body macrophages and elongated fibroblasts. 188(87%) of them were cytologically diagnosed as reactive hyperplasia of node, 26(12%) cases as malignant lesions. Out of 82 (23%) cases of tuberculous lymphod initis, 75(91%) were accurately diagnosed, and 7(9%) as non-specific hyperplasia which on histology proved to be tuberculosis. The cytological examination of smears in accurately diagnosed cases showed chiefly epitheloid cell aggregates surrounded by lymphocytes against a caseous background. langhans giant cells were seen in 27 cases only. Acid fast stain was done in 15 cases.

15 of 355 cases (4.3 percent) were lymphomas, they included 13 cases of non-Hodgkin's lymphoma (NHL)and 2 cases of Hodgkin's disease. Cytology of NHL smears showed relative homogeneity of cells and absence of tingible body macrophages and cells of myeloid origin. The latter showed polymorphic cells, including lymphocytes, eosinophils, macrophages and bi-nucleate or multilobate Read-Sternberg cells. Both cases of Hodgkin's disease were of mixed cellularity type. 14 of 15 (93 percent) cases were cytologically diagnosed as

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lymphoma while as 1 case (7%) was labelled as suspicious of malignancy. All except 4 cases of NHL were low-grade (Working formulation) and 4 cases were of intermediate grade malignancy.

Table-I

Showing type of lesions in relation with age (FNAC results of 355 cases ofLymphadenopathy Reported from 01-01-1995 to 31-12-1995

	Age In Years							
Cytologial diagnosis	0-10	11-20	21-30	31-40	41-50	Above 50	Total	%Age
(A) Inflammations								
(i) Hyperplasia (Non specific)	102	62	24	26	7	5	226	63.7
(ii) Granulomatous Lesion	8	29	18	15	8	4	82	23
(B) Malignancies								
(i) Lymphoma	-	-	-	2	8	5	15	4.3
(ii) Metastatic Carcinoma	-	-	-	-	18	14	32	9
Total	110	91	42	43	41	28	355	

32 cases (9.3%) were metastatic carcinoma. These were easily diagnosed (100%) by cytological examination by virtue of the presence of cells foreign to lymph node structure. 10 cases had known primary with subsequent lymph node enlargement. In 14 cases tumour was first diagnosed on FNAC. They included 2 cases each of papillary carcinoma thyroid, sqamous cell carcinoma lung, adenocarcinoma stomach and one case from each, hepatocellular carcinoma, adenocarcinoma lung, duct carcinoma breast, melanoma, acute myeloblastic leukaemia, nasopharyngeal carcinoma, squamous cell carcinoma-esophagus and seminoma arising from undescended testis. In 8 cases the primary site was not detected on cytology due to anaplasia of tumour cells.

Discussion

A wide variety of agents like bacteria, fungi, protozoa, viruses, autoimmune disorders, tumour antigens and AIDS-related disorders cause reactive hyperplasia of lymph nodes. The differentiation of reactive hyperplasia of node from NHL on FNAC is a challenge[1]. Smears from the former are reported to contain a polymorphic cell population, including small and large lymphocytes, macrophages and inflammatory cells, small to large lymphocytes in proportion of 80:20, small histiocytes 5 to 10 percent and large, poorly defined, tingible body macrophages. Smears from the latter are reported to be relatively monomorphic with alteration or reversal of small to large lymphocyte ratio and absence of large tingible body macrophages[1,5]. Abundant mitosis though associated with high grade lymphoma[1,6] have also been reported in infectious monoucleosus[7]. Cells resembling those of Reed-Sternberg cells have also been seen in tuberculosis, infectious monoucleosis and rubeola[8]. Phagocytosis though considerd a strong clue of inflamation is a noted feature of burkitt's lymphoma and at times is observed in other types of NHL also[1,6]. The diagnosis of Hodgkin's disease is more occurate due to the presence of a polymorphous infiltrate including lymphocytes, eosinophils and plasma cells. Presence of Reed-Sternberg cells is however diagnostic[1].

Table - II

Showing Relative Percentage of Inflammatory and Malignant lesions in Relation with Age. (FNAC Results of 345 Cases of Lymphadenopathy)

Age in Years	Inflammations	Malignancies
0-10	100	-
11-20	100	-
21-30	100	-
31-40	94	6
41-50	36.4	63.6
Above 50 yrs.	31	69

For the diagnosis of metastasis on cytology, the term "alien cells" was coined by Soderstrem[9]. The metastatic tumour cells usually resemble parent tumour cells. In 14 cases of metastasis from unknown primaries, we accurately detected the primary sites, in 8 cases primary site could not be made out because of marked anaplasia of tumour cells.

Table - III

Showing cytomorphological correlation (355 nodes)

		Diagnosis Cytologically reported		
Diagnosis	No of cases	Benign	Suspicious	Malignancies
1. Hyperplasia (Non specific)	226	87%	12%	1%
2. Tuberculous Lymphadenitis	82	91%	9%	-
3. Lymphoma	15	-	7%	93%
4. Metastatic Carcinoma	32	-	-	100%

Forkner described[10] eight aspirates from tuberculous lymphadenities with Langhan's giant cells, macrophages and epitheliod cells. Others have also made a diagnosis applying the same criteria[1,5]. However, acid fast staining is a confirmatory procedure for the diagnosis of tuberculosis[12]. We did not use acid fast stain to every case of tuberculous lymphadinitis. Since tuberculosis is common in Kashmir, so we considered every granuloma with cytological features of tuberculosis to be tuberculous lesion unless proved otherwise. Moreover all except one of these cases responded to antituberculous drugs. 52 percent of 1200 cases of lymphadenopathy reported by Zajicek et al were benign hyperplasia, 10 percent lymphoma and 38 percent secondary deposits of carcinoma. We had 63.7% cases of benign hyperplasia (non-specific) 4.3 percent lymphoma and 9 percent cases metastatic carcinoma in a total of 355 cases of lymphadenopathy. Kline et al in one series[15] of 130 cases of enlarged lymph nodes described 42 cases as benign hyperplasia of lymph nodes and 88 cases as malignant and in another series[1] of 376 cases, 137 cases as benign hyperplasia, 130 cases as metastatic carcinoma and 73 cases of lymphoma. These authors did not mention the ages of their patients. If we exclude lymphadenopathy of paediatric age group (which form 65 percent of present series) then our figures come in approximation with those of these authors. We had 23 percent tuberculous lympadenities as compared to 1.6 percent in the West[16] which could also be the cause of disparity. The striking observation in this study was that upto the age of 30 years all enlarged nodes were inflammatory in nature. Upto 40 years of age malignancies comprised 6 percent, in the age group 41-50 years 63.6 percent and in patients above 50 years they comprised 69 percent of lymphadenopathies (Table-II). The accuracy rate of cytological diagnosis in this series is similar to figures given by Kline et al.

Engzell et al after 5 years follow up of 641 cases with metastatic carcinoma diagnosed by FNAC found no evidence of recurrent tumour developing in the needle tract.

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Glucose-6-Phosphate Dehydrogenase Deficiency in Adult Kashmiris

Mohan Lal Bhat, MD; Raashda Parveen Chishti, MD; Bupindar Zutshi, MD; Asifa Rukhsana MD; Suraya Khan, MD; S. Manzoor Kadri. MBBS.

Abstract: 500 random patients were studied over a period of one year. Three cases of Glucose-6-Phosphate Dehydrogenase (G-6-PD) deficiency were observed (0.6%). Two cases were in the age group of 38-47 years and one was in the age group of 28-37 years. All the three case were males, which included two Sunni Muslims and one Sikh. The deficiency in these three cases was found to be compatible with life.

Key words: G-6-PD deficiency, Shia-Sunni, Sikh, Red cells

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Introduction

It has been known since long that certain ordinarily harmless drugs when administered to some individuals, result in acute haemolytic anaemia. Since 1926 it has been known that antimalarial drugs when administered to a G-6-PD-deficient person have a potential risk of developing acute haemolytic anaemia[1]. Various causes of this drug induced haemolysis were thought of and subsequently it was found that there is an intrinsic red cell abnormality of G-6-P D enzyme deficiency. It probably forms the most common metabolic error and is believed to be affecting hundred million people throughout the world[2]. It is well known that this enzyme takes part in the pentose phosphate pathway of red cell metabolism, hence its deficiency renders red cells susceptible to haemolysis.

Material and Methods

The study was conducted over a period of one year on a random group of 500 adults attending the central laboratory attached to SMHS Hospital and other associated hospitals of Govt. Medical College, Srinagar. These 500 cases included trainee technicians, medical and nursing students, blood donors and antenatal patients. Investigations carried out were haemoglobin-estimation, total leucocyte count, diferential leucocyte counts, reticulocyte counts and serum bilirubin levels. The screening of these 500 adults for detection of G-6-P D deficiency was done by Jacob and Jendle's method[3]. Out of these 500 random patients, 100 adults were tested additionally by methhaemoglobin reduction test[4].

Observation

The present study comprised of 500 adults, 490 patients (98%) were locals and only 10(2%) were migrants from other parts of the country. Age and sex distribution is shown in table 1 and 2.

Table I. Shows age distribution

S.No.	Age group in years	Total No.	Deficients	%age of G-6-P-D deficiency
1.	18-27	248	-	-
2.	28-37	131	1	0.7
3.	38-47	76	2	2.6
4.	48-57	24	-	-
5.	58-67	21	-	-

There were 229 males and 271 females

Table 2: Show sex distribution

Sex	Total No. of cases	%age	G-6-P-D deficiency	%age
Male	229	45.8%	3	1.3
Female	271	54.2%	-	-

These 500 random individuals included 434 Muslims (86.8%), 55 Hindus (11%) and 11 Sikhs (2.2%) Table 3. Among 434 Muslims 426 (98.15%) were Sunni Muslims, whereas 8 (1.84%) were Shia Muslims. Similarly, among 55 Hindus, 51 were Brahmins (92.7%) and 3 were Khatris (5.8%) and one belonged to a scheduled caste (1.8%). Among Skihs there were no subcastes.

Of the 500 adults only 3 cases of G-6-PD deficiency were observed. All the three were males comprising a percentage of 1.3% 2 cases (2.6%) were 47 years of

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age whereas one case (0.7%) was 32 years old.

Table 3. Shows religious distribution

S.No.	Religion cases	Total cases	%age of	G-6-P-D deficienty	%age cases
1.	Muslims	434	86.8%	2	0.4
2.	Hindus	55	11.00	-	-
3.	Sikhs	11	2.2	1	9

Two of the deficient cases observed in the study were Sunni Muslims out of 434 cases (0.4%) whereas only one case was observed among 11 Sikhs (9%).

The investigations carried in these 500 cases included haemoglobin estimation, total leucocyte count, reticulocyte count and serum bilirubin estimation. Two of the deficient cases had haemoglobin of 11-13 gms% whereas one had haemoglobin of 13-15gms%. Total and differential leucocyte counts were within normal limits. Reticulocyte count in these three deficient cases was between 0.7 to 0.9%. Serum bilirubin estimation was 0.6 mgms%, 0.7 mgms% and 0.8 mgms% respecitvely as shown in table-4.

Table 4

	Age (years)	Hb gms(%)	Reticulocyte count(%)	Serum bilirubin (mgms)	
Cases I	47	13-15	0.7 - 0.9	0.6	Direct - 0.2 Indirect - 0.4
Case II	47	11-13	0.7 - 0.9	0.9	Direct - 0.3 Indirect - 0.5
Case III	32	11-13	0.7 - 0.9	0.7	Direct - 0.2 Indirect - 0.5

Among these three deficient cases only one case had history of anaemia following administration of antimalarial drug whereas the other two had no such history.

Discussion

G-6-PD deficiency has worldwide distribution and is probably the most important inborn error of metabolism in man. Though primarily found in tropical and sub-tropical zones along the Mediterranean it is also seen eastwards through Middle East, India and China. The incidence reported from various countries is: China 5.5%[5], Pakistan 2.3%[6] and Libya 17.1%[7]. In India a considerable variability incidence of enzyme deficiency has been reported. In Parsees of Bombay a total percentage of 15.5[9] was reported by Baxi et al. Other authors have reported an incidence of 12.7% and 27.0%[9,10]. Naga adults and children have an incidence of 3.5% as reported by Dube et al[11]. The lowest incidence of 1.3% has been reported among adult Dravidians from Kerala by Saha et al[12].

In the present study a prevalence of 0.6% has been observed. Our observations are quite close to that of Saha.

The great variability in the incidence of G-6-P D deficiency in this country may be attributed to genetic diversity and complexity of population. The low prevalence rate of G-6-PD deficiency in this part of the country (Kashmir valley) may be attributed to different climatic environment and near complete absence of malaria. The higher incidence of malaria in the rest of the country may be responsible for the higher incidence rate of G-6-P D deficiency as it has been reported to induce the deficiency and hence G-6-P D deficient cells are resistant to malaria[13].

The prevalence rate of 0.6% of G-6-P D deficiency was found only in local Kashmiris and none in the migrants from other States in the Valley which were included in the study. The two deficient cases (2.6%) were of the age of 47 years and one case (0.7%) was of the age of 32 years. All the three were males and these observations were in conformity with Baxi (08) who has reported an incidence of 19% in males whereas Mittal has reported 5.6% in males. The higher incidence of G-6-P D deficiency in men is determined genetically and is transmitted along x chromosome. None of the three deficient cases were products of consanguinous marriages though in this study 231 adults were born of consanguinous marriages. It is therefore well maintained that products of consanguinous marriages may not necessarily be G-6-P D deficient cases.

Conclusion

The prevalence of G-6-P D deficiency in Kashmir valley is lowest (0.6%) as compared to other parts of the country. The low prevalence of G-6-P D deficiency in this part of the country is attributed to climate and environmental factors, pollution free atmosphere as well as well as near total absence of malaria.

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Comparative Evaluation of Relative Dissolution and Disintegration Profiles of Seven Commercial Cotrimoxazole Brands

Z.Jeelani MD. DM.; Z.A. Wafai MD; Farhat Shawl M.Sc.

Abstract: *Seven commercial brands of sulfamethoxazole and trimethoprim combined in the form of uncoated tablets, were obtained from the market and investigated for dissolution and disintegration properties. Six brands contained an average of 92.57% (88.50% to 95.21%) and one (Cotrimoxazole DS) contained 82.48% of the labelled drug. The disintegration time of this brand was 20 minutes while that for other six brands varied from 4 to 10 minutes.*

Key Words:- *Sulfamethoxazole, Trimethoprim, Rate of dissolution, Disintegration time, Bioavailability*

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Introduction

The absorption, regardless of site, is influenced greatly by various physico-chemical properties of a drug. Particle dispersion and solubility for solid dosage forms are known limiting factors for absorption[1]. The combination of Trimethoprim and Sulphamethoxazole on 1:5 basis in uncoated tablet form is widely used for systemic treatment of bacterial infections. Physico-chemical properties of its different formulations by different manufacturers indicate marked variability[2]. On one hand, dissolution rate of sulphamethoxazole itself in suspension form has shown considerable variability and on the other hand, the influence of pH of dissolution medium is enormous. Sulphamethoxazole (analogue of p-aminobenzoic acid) being weakly acidic, is poorly soluble in acid medium whereas trimethoprim is readily soluble. Therefore, sulphamethoxazole in cotrimoxazole tablet was used as determinant of absorption, influencing bioavailability. Seven different commonly used brands of co-trimoxazole in tablet form were included in this study to predict their extent of bioavailability.

Material and Methods

The commercially available Septran, Mortin DS, Co-trimoxazole DS. Bactrim DS, Sepmax, Lorato DS and Trisulfose DS were randomly obtained from the market and studied for their relative disintegration and dissolution profiles in vitro in a representative intragastric acid medium (pH 4.8-5.2). Solubility of sulphamethoxazole in these combination tablets was studied in dissolution rate test apparatus, using 900 ml of 0.1 NHCL[3] with Na_2HOP_4 and NaH_2PO_4 buffer[2] as dissolution medium. Each tablet was caged into tablet box, stirrer adjusted at 100 rpm and temperature maintained constant at 37°C throughout the experiment. Five ml of medium were withdrawn after 5 minutes, 10 minutes and thereafter every 15 minutes, filtered and analysed for sulphamethoxazole concentration. Equal volume of fresh 0.1 NHCI in buffer was added to the dissolution medium every time to replace the volume.

For every brand, 3 tablets were tested in each sitting and the mean percentage of sulfamethoxazole dissolved was plotted against time to find the comparative extent and rate of dissolution of these products. Standard sulphamethiazole for comparison was obtained as powder from SIGMA Chemicals Co.

The estimation was done by the calorimetric method based on quantitative formation of a diazo compound by reaction of sulphamethoxazole with pure N (1-naphthyl)-ethylenediamine[4]. The amount of drug dissolved per dl. of dissolution medium was calculated from absorbance versus concentration curve and reading record at 535 nm.

The tablet disintegration time was recorded in 0.1 NHCl plus buffer at 37 ± 0.5°C using tablet disintegration test machine, IP Standard Bells Ltd.

Results

Sulphamethoxazole was found to be contained in all the seven brands. Six brands contained 88.50% to 95.12% and one contained 82.48% of the labelled amount of drug (Table and Fig.1).

The dissolution study showed that sulphamethoxazole was freely soluble in 0.1 NHCI when the pH was adjusted to 4.8-5.2 by adding buffer. The represented optimum pH in intragastric environment after taking food when this drug is mostly used by patients in our set-up. The

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dissolution was nearly complete at 2 hours (Fig. 1).

The disintegration time of tablets varied from 4 minutes to 10 minutes but Cotrimoxazole DS took 20 minutes to disintegrate (Fig.2)_. The maximum disintegration time specified in I.P. being 15 minutes.

The disintegration and dissolution of cotrimoxazole DS showed a related pattern. This drug had longer disintegration time and lower rate and extent of dissolution than other brands studied.

Table

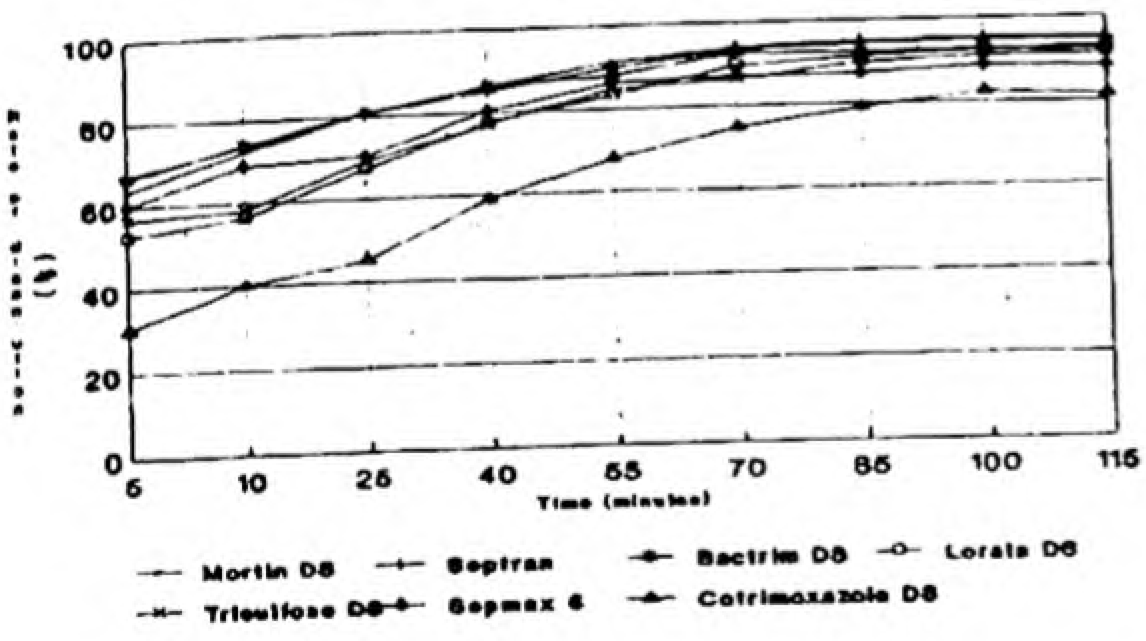
Rate of Dissolution % of Seven Different Brandsof Cotrimoxazole

Time (min.)	Mortin DS	Septran	Bactrim DS	Lorato DS	Trisulfose DS	Sepmax	Cotrimoxazole DS
5	63.71	67.50	66.83	52.87	56.70	60.09	30.59
10	72.42	73.61	74.01	56.51	58.28	69.07	40.20
25	80.66	80.53	80.80	67.50	69.27	70.53	47.54
40	86.20	85.09	86.36	77.55	77.00	80.51	80.09
55	91.25	90.07	88.18	83.56	84.91	86.29	71.08
70	94.36	92.50	93.02	89.90	86.53	87.56	76.09
85	95.12	94.51	92.54	91.55	90.06	87.50	79.09
100	95.20	94.88	93.01	92.50	91.34	88.99	82.48
115	95.21	94.79	93.10	92.49	91.35	88.50	81.49

Discussion

The investigation of two important physical properties: Tablet dissolution and disintegration of market preparations of sulphamethoxazole and trimethoprim is done with the objective to get information to predict variation and extent of possible bio-availability of these drugs.

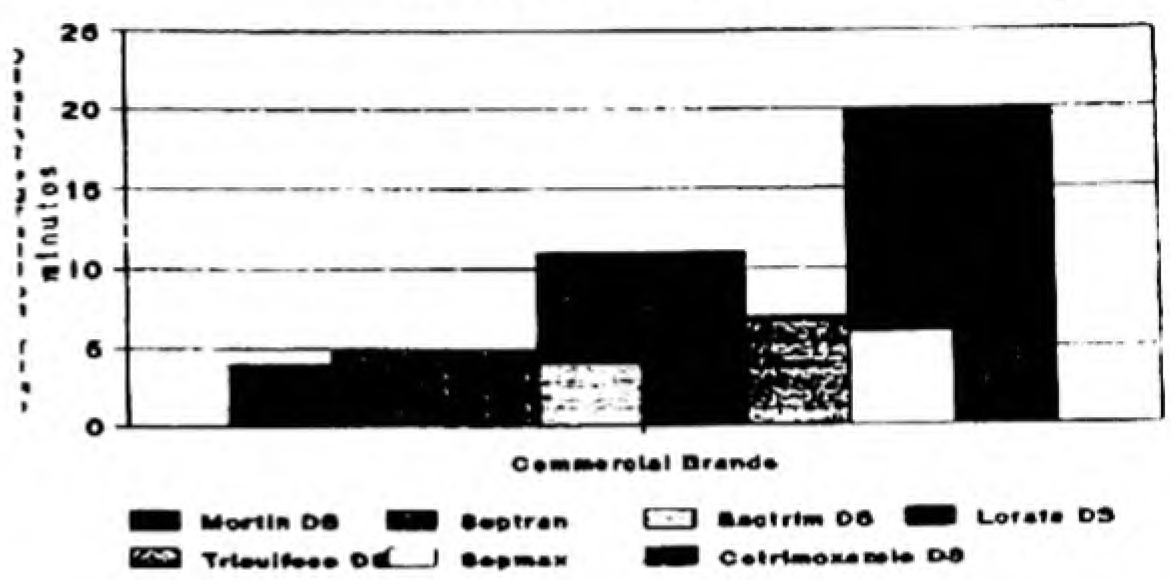
Fig. I Rate of Dissolution of seven different commercial cotrimoxazole brands



Solid drug dosage forms administered orally for systemic activity must dissolve in gastrointestinal fluids prior to absorption. The pH of gastric fluids exerts a great influence on what happens to that dosage form and on its pattern of absorption. Gastric acidity shows marked diurnal variation. Though constantly more towards acidic side during the night, pH remains fluctuating from 1 to 5 during the day[5].

Since dissolution and disintegration are pre-requisite steps for absorption and are often slow and rate-limiting processes especially for poorly soluble drugs like sulfamethoxazole, pH will exert a major influence on the over-all absorption process. Small intestine being the major site of absorption, it seems that sulfamethoxazole, a poorly soluble drug must first dissolve in the acidic gastric juice in order to be well absorbed from the intestine.

Fig. II Disintegration Time (Min) of seven commercial cotrimoxazole brands



We have limited the infleunce of pH variability by maintaining it at 4.8 to 5.2 in order to limit our investigation to observe the dissolution and disintegration profiles at the optimum range of gastric pH after food.

Trimethoprim being basic in nature[6], is highly soluble in acidic medium and rapidly absorbed[10]. Sulphamethoxazole is poorly soluble[3]. It is expected to show great variation in absorption. We therefore, adopted the sujphamethoxazole dissolution rate test as an index to preclude the bioavailability of sulphamethoxazole and trimethoprim combined in a tablet form. Sulphamethoxazole dissolved at different rates upto 82.48% to 95.21% of the amount labelled on the tested brands (Table and Fig 2).

Finholt 1974 studied the dissolution of phenacetin granules prepared using different seive fractions of the drug powder. The rate of drug dissolution increased with decrease in particle size[7]. Differences in the dissolution rates and solubility of different polymeric forms of a given drug are well documented[8]. The dissolution rate of the drugs is most rapid from tablets containing a compressible starch[1,8]. Thus the observed differences in the dissolution of sulphamethoxazole in these commercial forms may be due to formation and manufacturing variables such as particle size, physical forms, solubility, type and quantity of excipients, polymeric forms and compression pressure etc.

The purpose of disintegration is to facilitate the break-up of tablet after its administration exposing the particle surface area for dissolution. Our results indicate that disintegration and dissolution of the seven brands show a related pattern. Disintegration for Cotrimoxazole DS was delayed to 20 minutes as compared to other six brands, which showed disintegration time from 4 to 10 minutes (Fig.2), well within 15 minutes as specified in I.P. for uncoated tablet[9].

In conclusion it is possible that sulfamethoxazole alone or including trimethoprim from co-trimoxazole DS may not be available to tissues as much as from other brands, for antibacterial effect. To know whether the concentration (82.48%) is effectively antibacterial and/or maintained for longer periods in vivo due to its slow disintegration and dissolution, warrants further investigations.

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Spontaneous Rupture of Umbilical Hernia in Refractory Ascites Leading to Improvement in Clinical Condition

Chirag Parikh MD; Showkat Bashir MD; Samia Qazi MD; Laurie Ward MD, FACP

Abstract: *Refractory ascites in patients with end-stage liver disease is a difficult problem to manage. Large-volume paracentesis is often used for the control of the ascites and its associated symptoms, such as respiratory distress. Such an approach is not ideal in that it can cause systemic volume and electrolyte abnormalities, as well as precipitate hepatorenal syndrome. We report a case of intermittent spontaneous paracentesis through a ruptured umbilical hernia with improvement in clinical condition. The patient is a 44-year-old male with Child's Class C cirrhosis, secondary to chronic hepatitis B and C as well as alcohol abuse. He had a number of hospitalizations for tense ascites, and encephalopathy requiring ICU monitoring on two occasions in the past. The patient was hospitalized with tense ascites, and was noted to have a 4x4x6 cm umbilical hernia. The tension in the hernia was used as a marker for intra-abdominal pressure and this, along with respiratory distress, was used as a guide for timing of therapeutic paracentesis. Over the first three weeks of the hospital stay, approximately 12 liters were removed over three occasions. The patient required transfer to the ICU twice for encephalopathy that was temporally related to her paracenteses. Then, the hernia ruptured and a 0.5 cm hole formed in the skin. Ascitic fluid drained rapidly at first, and then the rate decreased. Surgical repair was not felt to be feasible due to poor general condition and persistent ascites which would make healing unlikely. A colostomy bag was placed over the hernia rupture site, and it was noted to drain a variable amount daily, presumably based on the intra-abdominal pressure. His condition improved dramatically, and he had no further episodes of encephalopathy or necessity for ICU transfer, and was able to be discharged within one week of hernia rupture. He did have one episode of peritonitis the day after the rupture, which was easily treated wih antibiotics and has not recurred at the time of last follow-up. Conclusions: 1) In this patient, daily small-volume paracentesis was better tolerated than intermittent large-volume paracentesis; 2) This case may provide insight into possible new therapeutic modalities that mimic this spontaneously occurring pressure-regulated valve.*

Key words: *Umbilical hernia, Refractory ascites.*

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Case Report

A 44 year old white male with a history of liver cirrhosis secondary to chronic hepatitis B & C as well as alcohol abuse was admitted with progressive distension of his abdomen, difficult breathing and some mental status changes. There were no complaints of fever, abdominal pain or any drug abuse. On physical examination his pulse was 70 beats/minute, blood pressure was 100/60 mmHg with a respirtory rate of 26/min. He was afebrile. Signs of chronic liver disease like parotid swelling, spider naevi, gynecomastia were easily appreciated. His chest and cardiovascular examination were unremarkable. Abdominal examination revealed tense ascites interfering with the palpation of organs. There was a 4 x 4 x 6cm, polyp like umbilical hernia, the skin over the latter being so thin and shiny that loops of intestine could be seen through it. Mental status was normal and there were no focal deficits. There was mild peripheral edema over the extremities. Laboratory evaluation showed a hemoglobin of 8.4gm/dl, hematocrit of 24.1%, platelets of 149,000/cmm with a peripheral leukocyte count of 7,100/cmm. The serum electrolytes were within normal range, however albumin was 1.7gm%. The renal profile showed blood urea nitrogen of 30mg% and creatinine of 1.7mg%. The liver function tests indicated a bilirubin of 3.7mg%, AST of 120 IU/L, ALT of 86IU/L and alkaline phosphatase of 156mg%. Diagnostic paracentesis proved the ascitic fluid to be a transudate.

The course in the hospital which has been graphically demonstrated in Figure 1 was as follows:

Week 1: Paracentesis was done on 3 occasions and 3-4 liters of fluid removed each time. Breathing improved to some extent.

Week 2: Patient developed hypotension and mental

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status changes requiring transfer to ICU.

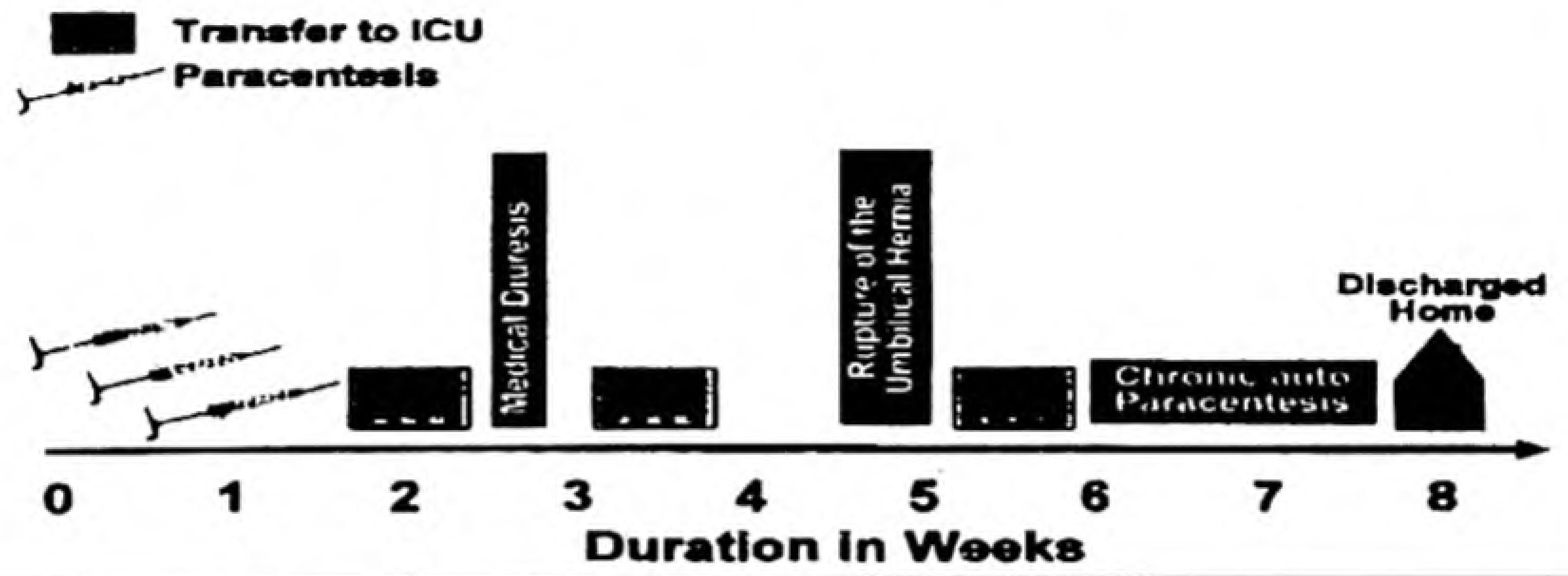
Week 3: Distension worsened and breathing was compromised once again. This time the doses of diuretics (lasix and spironolactone) were maximised.

Week 4: Required ICU for management of encephalopathy.

Week 5: Umbilical hernia perforated and patient lost about 10-12 liters of fluid. Abdominal distension reduced markedly. Once again went into hepatic encephalopathy and was transferred to the ICU. Also developed bacterial peritonitis which was easily treated with antibiotics. Surgical consultation was obtained and the opinion was that surgical repair was not feasible because of medical condition of the patient and uncontrolled ascites which would interfere with healing. The umbilical hernia was covered with a colostomy bag, to prevent infections.

FIGURE - 1

Schematic Representation of Course of Stay in Hospital



Week 6-8: The patient had no further episodes of respiratory distress, encephalopathy or peritonitis. Clinically, marked improvement was noted. He spontaneously drained variable amounts (300-400 cc daily), presumably based on intra-abdominal pressure, through the hernia site. The patient was able to be discharged on day 56 with a colostomy bag over the hernia site.

Discussion:

There is an increased incidence of abdominal hernia including umbilical hernia, in patients with cirrhosis and ascites. The reported overall incidence of abdominal hernia in cirrhosis is 10% which increases to 40% in the presence of ascites[1]. Umbilical hernia is believed to occur in such patients as a result of increased intra-abdominal pressure causing herniation of abdominal contents through congenital latent defect in the abdominal wall[2].

The complications of umbilical hernia are mainly leakage, ulceration, rupture and incarceration. Most of these complications occur when the intra-abdominal pressure increases with accumulation of ascitic fluid. However, incarceration appears to occur with sudden decompression of tense ascites[3]. In cases of chronic cirrhosis with ascites, periodic paracentesis is an important part of management. Most of such cases progress to refractory ascites when need for aggressive diuresis & repeated hospitalizations and complications become evident. This in turn, adversely affects the quality of life and enormous expenses are incurred with little or no benefit.

Our patient illustrated typical course of a terminally ill patient with cirrhosis and ascites requiring repeated hospitalizations, multiple transfers to intensive care unit till the time of a spontaneous rupture of his umbilical hernia. Subsequently, the course of his disease stabilized and he could be discharged with no further hospitalizations. However, it is prudent to mention here that such patients become more prone to peritonitis. One approach that has been tried to prevent this is by using an almunium strip taped to the abdominal wall. A thin almunium (1/8th inch) strip measuring 1.5"x5" and coated on its skin layer with a thin layer of sponge is strapped across umbilical hernia site with elastoplast. The site is checked every 48 hrs. cleaned and new elastoplast used[4].

This case exemplifies the conservative cost-effective management of cases of refractory ascites who develop ruptured umbilical hernia. In fact this may provide an insight into possible new therapeutic modality that mimic this spontaneously occuring pressure regulated valve.

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Sick Sinus Syndrome Associated with Generalised Neurofibromatosis

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Abstract: *We are reporting a case of Generalised Neurofibromatosis associated with Sick Sinus Syndrome necessitating a permanent pacemaker implantation. To our knowledge such an association has not been reported in the literature so far.*

Keywords: Sick sinus syndrome; Neurofibromatosis.

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Case Report

A sixty years male presented with recurrent syncopy unassociated with convulsive movements or any focal neurological signs except for the evidence of generalised neurofibromas with cafe au lait spots, on trunk and extremities, Blood pressure recodings were normal all along. There were no signs of cardiac failure.

Investigations revealed normal Haemogram, Urine analysis, BUN, Electrolytes. Urinary VMA estimation was normal.

E.C.G. at the time of first presentation revealed intermittent sinus arrest with Junctional escape and intermittent sinus pauses; logest pause being 2.5 sec. There were no electrocardiographic signs of myocardial ischemia, infarction or cardiac chamber enlargement. Atropine test performed prior to pacemaker implantation showed a basal sinus bradycardia with a rate of 45 bpm. Atropine sulfate was given in a dose of 0.04 mgs/kg body weight and sinus rate increased to 55 bpm at 5 min and 10 min. X-Ray Chest revealed a cardio-thoracic ratio of 45% without any radiological signs of pulmonary venous hypertension or pulmonary arterial hypertension. Two dimentional echocardiography revealed a structurally normal heart with normal left ventricular function. Cranial CT was normal. EEG showed a normal graph. After implantation of permanent pacemaker subsequent ECG's revealed intermittent paced rhythm and patient was free of syncopal episodes on follow up.

Discussion

The association of phaeochromocytoma and neurofibromatosis is well documented though uncommon. Sick Sinus Syndrome has not been reported as an association of either type I or type II neurofibromatosis. It is difficult to speculate as to what pathophysiological mechanisms could be responsible for Sick Sinus Syndrome in our patient. Alternatively occurence of Sick Sinus Syndrome could be a chance finding in this patient. Rarely neurofibroma could be found in the heart and produce heamodynamic abnormalities or rhythm disturbances. But absence of suggestive clinical features and normal echocardiographic study rules out such a diagnosis in this patient.

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Agenesis of Hemidiaphragm - Repair by Prosthetic Material

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***Abstract**: Six cases of agenesis of diaphragm were operated in our Institute over a period of 8 years in the department of Cardiothoracic and Vascular Surgery. Two patients did not have a preoperative diagnosis while as four patients were diagnosed by flouroscopic screening of chest. All the patients presented with nonspecific symtoms of pulmonary compression.Liver was seen projecting in to the right pleural cavity in all patients covered over by a thin layer of loose areolar tissue. Herniation of liver was reduced in all by mobilising the tissues around it. Proline mesh was used to cover the defect in all the patients. Incomplete reduction of quadrate lobe was achieved in one patient. One patient had postoperative collection of serous fluid underneath the mesh which resolved conservatively. All the patients improved subsequently with no morbidity or mortality. Our experience with these cases suggests the probability of this defect in doubtful cases of shadow (R) lower zone of chest with inconclusive serological tests. It is thus important to keep things available for reconstruction of diaphragm in such doubtful cases.*

***Keywords:** Agenesis; Diapharagm; Surgical Repair*

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Introduction

Lower zone pulmonary mass lesions are very common shadows seen on plain radiography of chest. Although age and clinical status of patient, location and contour of the lesion, serological and other radiological tools help a lot in the management of a pulmonary mass lesion but there are occasions when such a lesion is not diagnosed before the pleura is entered by a thoracotomy or during a thoracoscopic incision.[1] It is even necessary to keep a frozen section facility at hand while exploring such a lesion. On the other end of the spectrum lies a mass lesion (R) lower lobe with all investigations either inconclusive or borderline positive. Subpulmonic effusion, suprdiaphragmatic lipomas are the usual preoperative diagnosis in such patients[2,3,4]. Very rarely the diagnosis of herniation of an abdominal organ through a rent in the diaphragm strikes the clinician. Even if it does, it is very difficult to label a patient with certainty with such a rare disease. Moreover it is very difficult ordinarily to confirm the diagnosis by any means even by flouroscopic examination of the diphragmatic movements[5,6]. Most of the times it is a peropertive finding and is to be managed according to the finding on table.

Material and Methods

Case I

A 28 year female patient presented with non-specific symptoms of chest discomfort on (R) lower chest, dry cough of 1 yr. duration. Patient had occasional pain over (R) shoulder. She was treated for brachialgia by orthopedicians. Ultrasound did not help much but only ruled out a biliary pathology. X-ray chest showed a globular shadow over (R) lower lobe (fig. 1). Casoni's test and hydatid serology were inconclusive. Due to prevalence of hydatid disease in the region, the patient was opened as a case of hydatid cyst through (R) post-lateral thoracotomy incision but surprisingly, the lung was free while as the (R) lobe of liver was seen projecting into the pleural cavity. There was a thin rim of diaphragm around the liver on (R) side. Liver was bound to the diaphragm by thin adhesions. Diagnosis of agenesis of (R) hemidiaphhragm was made and the liver was mobilized and reduced to the peritoneal cavity. The gap was repaired by a proline mesh sutured by proline suture (Fig.2). Chest was drained by a tube connected to under waterseal drainage system. The post operative period was ueventful and patient discharged home with no morbidity. On follow-up she is symptom-free and x-ray chest is normal.

Case II

A 25 year male patient with similar presentation as that of first patient, he also went through the same battery of investigations. X-ray chest was showing a globular shadow above (R) diaphragm. Rest all the investigations were giving the same result as in the first case.

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Flouroscopy revealed a mass continuous with liver moving into the right pleural cavity. He was labelled as a case of herniation of liver into pleural cavity but with doubt. On operation, he proved to have the same lesion as suspected and managed in the same way. Results are also the same. Follow-up reveals no morbidity and the patient is symptom free.

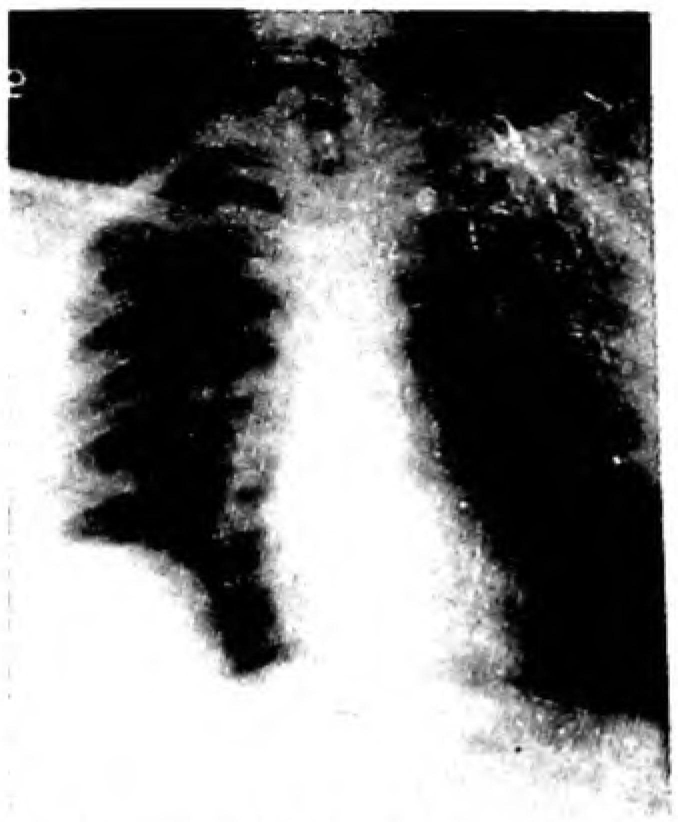

Fig. I Radiogram chest showing a mass lesion in the Rt.-Supradiapharagmatic region

Case III

A sixteen year female had fever and consolidation over lower lobe of (R) lung which was treated and x-ray chest revealed a persistent shadow over right base. It was investigated and CT chest revealed a ecohogenic mass continuous with liver and projecting into the pleural cavity. She was opened with a preoperative diagnosis of herniation of liver into the pleural cavity. On operation, her superior surface of (R) lobe of liver was seen multilobed and one part was herniating into pleural cavity through a wide deficiency in the (R) hemidiaphragm. This too was reduced and the defect repaired by proline mesh. Post-operatively, she had subpulmonary collection which was aspirated under the guidance of ultrasound. She is under our OPD follow for five and half years and is asymptomatic.

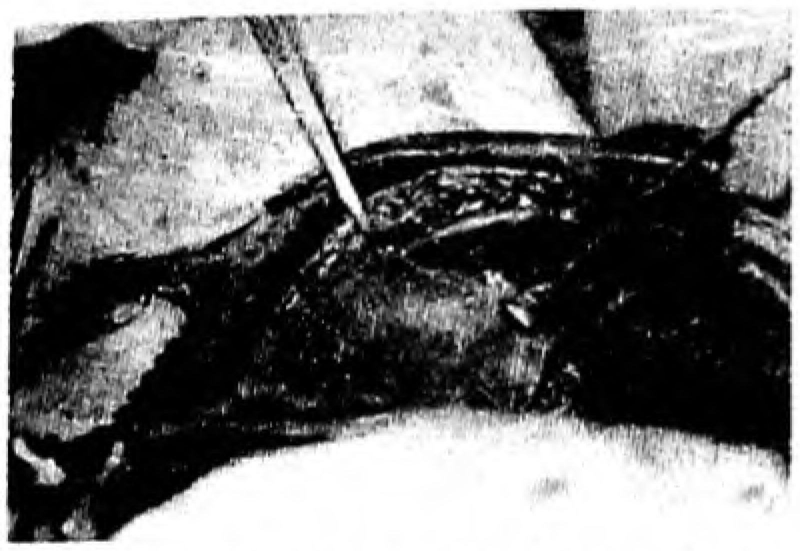

Fig. II Peroperatively a prolene mesh was used to repair the diapharagmatic defect.

Case IV

A 22 year old male and a x-ray chest for a nonspecific cough and fever. It revealed a globular shadow over the base of left lung. He was treated with an imperative diagnosis of infected hydatid cyst. Casoni's test and hydatid serology were doubtful. USG abdomen showed a normal study. On exploring the left pleural cavity, spleen was seen protruding into a rent in the left hemidiaphragm with dense adhesions around it. It was mobilized and reduced into the peritoneal cavity. The defect was repaired by a proline mesh. The patient is operated more than 3 years before now with no complaints on follow-up.

Case V

A 45 year female with a mass lesion (R) lower chest was screened for hydatid disease. She had a postivie casoni's test. Flouroscopic examination revealed the mass rising up during expiration and staying in pleural cavity during the inspiration. Thus she was also explored doubtfully and proved to have agenesis of diaphragm. Material and methods for repair of diaphragmatic rent were same as in other patients. Results are satisfactory during a after follow-up of 37 months.

Case VI

A 19 year old female with a CT diagnosis and flouroscopic evidence of agenesis of diaphragm was operated 2 months before by the same method and proline mesh was used again for the repair. The liver could not be fully reduced into peritoneal cavity but there are no compressive symptoms experienced by the patient after surgery.

Discussion

Mass lesions of lung pose a very difficult problem to diagnosis especially in young children[3]. It is very difficult to differentiate between a malignant and a benign lesion and separating different benign lesions from each other is also not easy. Although plain radiology, biochemistry and contrast CT scanning of chest help a long way in evaluating a mass lesion of lung, it is often very difficult to draw a line between liver and (R) lower lobe mass lesions of lung[7].

As shown in the material and methods, it is evident that none of the patients was above the age of 45 years. So there was no suspicion of having a malignant lesion in any of the patients. Hydatid disease being more rampant in this part of the world, was considered first and patient got investigated accordingly. Bronchoscopy was performed only in three patients. All the three examinations were normal. Patients had mass lesions (R) lower lobe near the hilum[8]. All the three examination were normal. Serology for hydatid disease was positive in one and doubtful in another. The false positive test although very rare is known. It could be explained again on the basis of hydatid disease somewhere else in the body. Doubtful serology is also explained in the similar manner. CT scan of chest could only furnish a morphological diagnosis. Two cases were diagnosed by flouroscopic examination of the diaphragm. This may also not help always as the lower lobe lesion of lung adherent to diaphragm can also be confused with herniation of liver spleen[9].

Operating a doubtful lesion like this makes us wiser to consider agenesis of diaphragm although very catiously and keep things at hand while operating[4].

Different materials have been tried for the repair of agenesis of diaphragm. We preferred proline mesh as it is a non irritant, non absorbable, and strong. We did not try any other material[4].

One patient who got a subpulmonic collection responded to conservative method showing thereby that the collection has been only reactionary and non-infective[9]. The follow up of these six patients is now 8 years in one patient. More than 5 years in 2 patients, 3 years in 2 patients and one patient is operated 2 months before[10]. There is no complaint related to the procedure in any patient and the pulmonary compressive symptoms are abated. X-ray chest reveals a persistent shadow in (R) lower chest is one patient but the size of shadow is significantly smaller and flouroscopy has revealed no movement of liver into the chest[12,11]. This is explained on the basis of mesh being a strong barrier between chest and abdomen[11]

Although agenesis of diaphragm is a rare disorder associated with herniation of abdominal organs into the chest as compared to the hernias through small formina of diaphragm yet it is wise to consider it as a posssibility in a right lower lobe shadows of chest especially when the investigations are inconclusive[12,13]

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Congenital Lobar Emphysema: A Rare Cause of Neonatal Respiratory Distress

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Abstract: Congenital lobar emphysema is a rare cause of respiratory distress in a newborn baby. We report a 4 days old male neonate who presented to us with respiratory distress since birth. Chest radiography of the neonate revealed congenital lobar emphysema involving left upper lobe. Patient's condition deteriorated rapidly after admission. An emergency left upper lobectomy was performed which was life saving.

Key Words: Lobar emphysema, Lobectomy, Respiratory distress.

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Introduction

All neonates with respiratory distress need immediate evaluation to identify any underlying surgical cause like- congenital diaphragmatic hernia, oesophageal atresia with tracheoesophageal fistula, congenital cystic adenomatoid malformations of lung or congenital lobar emphysema[1].

Congenital lobar emphysema is a rare cause of neonatal respiratory distress and usually presents as an extreme emergency[1]. The chest radiograpy is characteristic and only rarely are other investigations (CT scan, radioisotope lung scan) indicated[1,2]. Treatment is surgical in the form of lobectomy[1,3].

Case Report

A 4 days old male neonate presented with dysponea since birth. Physical examination revealed tachyponea, diminished breath sounds and hyperresonant percussion note over left side of. chest. Apex beat ws shifted towards right. Chest radiograph showed a hyperlucent, overexpanded left upper lobe, with collapse of left lower lobe and marked mediastinal shift. These findings are characteristic of lobar emphysema. There was no associated anomaly.

Fig. I: Radiogram chest showing emphysmatous Lt. upper lobewith collapsed lower lobe with gross mediastinal shift

After admission in the hospital, patient's condition deteriorated rapidly and therefore the baby was taken up for emergency surgery. A posterolateral thoracotomy through 5th intercostal space was performed. The left upper lobe was found to be hyperinflated and did not deflate on compression. Left upper lobectomy was performed. Post-operatively patient was put on ventilator and was extubated on 2nd post-operative day. Post-operative chest radiography showed well expanded left lower lobe and normal mediastinal contour. Patients was discharged on 10th post-operative day.

Discussion

Congenital lobar emphysema is a rare condition in which massive overinflation of usually a single pulmonary lobe occurs as a result of air trapping and the affected lobe cannot deflate normally. The basic pathology being bronchomalacia, a deficiency of bronchial cartilage which results in collapse of the bronchi when surrounded by positive intrapleural pressure[1,3]. The overinflation of a single lobe leads to collapse of adjoining lobe and mediastinal shift. Fifty percent of the cases appear in first 4 weeks of life and the remainder later in infancy[1]. The lobes most commonly affected are left upper, right middle and right upper in that oder[1,5]. Partial obstruction of the bronchial lumen by inflammatory exudate or aspirated mucus may also cause lobar emphysema during neonatal period[1,4]

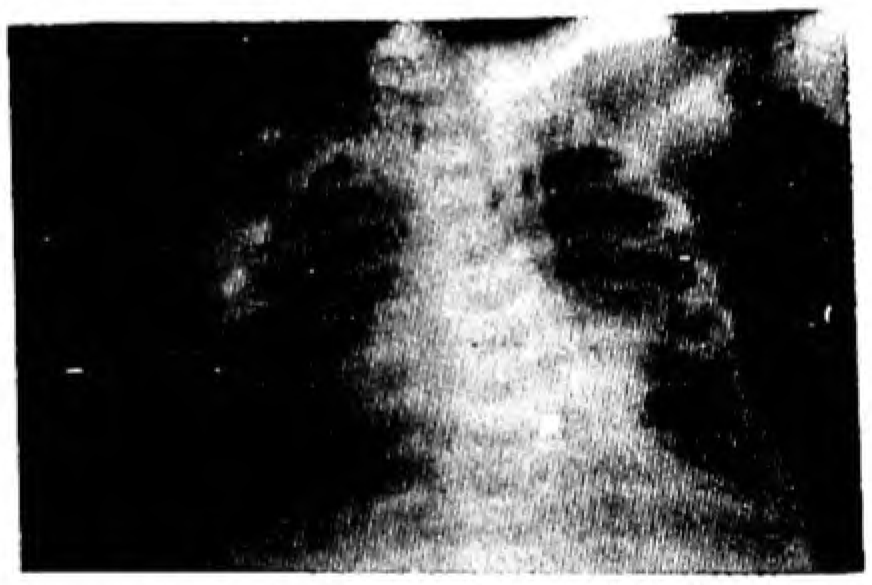

Fig. II Post operative radiogram chest showing expanding left lower lobe.

Chest radiography is usually sufficient to establish a diagnosis only in doubtful cases. CT scan or radioisotope lung scan is needed[1]. Treatment of congenital lobar

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emphysema is surgical in the form of lobectomy[1,3].

Our patient also presented as an emergency. The diagnosis was established by a chest radiography and the patient was treated successfully by lobectomy.

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Tubercular Meningitis with Amenorrhoea Galactorrhoea Syndrome

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Abstract: CNS tuberculosis can present with variable clinical features, although tubercular meningitis is the commonest presentation, it can also present as space occupying lesion (Tuberculoma) in any region of brain. The clinical picture will be determined by the size and site of tuberculoma. Symptoms are often limited to seizures. Fever and systemic toxicity are rare. Endocrinopathies may become evident months or years after the recovery from tubercular meningitis, most likely due to progressive scarring of the hypothalamus or a tuberculoma pressing the stalk.

We present a patient with an unusual complication of CNS tuberculosis as Amenorrhoea-Galactorrhea syndrome.

Key Words: Amenorrhoea, Endocrinopathy, Galactorrhoea, Space Occypying Lesion (SOL), Tuberculoma.

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Case Report

35 years old female married having 2 issues with regular menstrual cycles presented with history of low grade continous fever, vomiting, altered sensorium of 2 weeks duration. Examination revealed a conscious, irritable patient with features of meningeal irritation and papilloedema. Rest of the examination was unremarkable. Investigations included normal complete blood counts (CBC), urine examination, X-ray chest and electrocardiogram. She had normal serum urea, creatinine, bilirubin, liver enzymes and electrolytes, sterile blood cultures twice after 48 hours of incubation. Montoux test was positive-16 mm after 72 hours. Examination of cerebrospinal fluid (CSF) revealed total leukocyte count (TLC) of 110 cells/ml. Differential leukocyte count (DLC) mostly lympocytes, proteins 72 mg/dl, suger 34 mg/dl and smear was positive for acid fast bacilli. CSF culture sensitivity was sterile after 48 hours and CSF for malignant cells was negative. Cerebral blood flow and static brain scan done with 99mTc did not show any definite SOL. Patient was put on 9 months antitubercular regimen with initial 2 months of 4 drugs regimen (INH 300mg, Rifampicin 600mg, Ethambutol 800mg and Pyrazinamide 1.5g OD) and 7 months of 2 drug regimen (INH 300mg, Rifampicin 600mg OD). Patient tolerated treatment well. Repeat CSF examination after 10 days revealed TLC only 8 cells, all lymphocytes, proteins 30 mg/dl and sugar 45 mg/dl, almost normal CSF examination. Patient continued this regimen for 9 months recovered completely and was alright till September, 1995.

Patient got re-admitted in February, 1996 with complaints of severe frontal headache, blurred vision and milky discharge from breasts associated with breast discomfort and secondary infertility of one year duration. Examination revealed patient conscious, normotensive, vitals stable, galactorrhoea positive, fundus examination revealed optic atrophy bilaterally and rest of the examination was unremarkable.

CSF examination showed TLC 15 cells/ml. DLC - mostly lymphocytes, proteins 60 mg/dl, sugar 38 mg/dl, Gram stain and AFB staining was negative. CSF culture sensitivity sterile. Other investigations showed Montoux test positive (10 mm), ELISA for TB positive, sputum for AFB negative thrice and gynaecological checkup normal

Hormone Profile		Normal Values
FSH	2 IU/L	(5-20 IU/L)
LH	<3.00 IU/L	(5-25 IU/L)
Prolactin	200 ug/L	(<20 ug/L)
T3	1.8 nm01/L	(1.1-2.9 nm01/L)
T4	97 nm01/L	(64-154 nm01/L)
TSH	3.2 mu/L	(0.4-5 mu/L)

CT scan brain showed multiple isodense lesions in midbrain and supra sellar region, lesions were surrounded by mild oedema with post contrast enhancement of lesions. Diagnosis of tuberculomas brain was made (Fig. 1).

Patient was put on ATT in view of clinical and investigative evidence of tuberculosis. Patient received 12 months antitubercular treatment (ATT) 2 months 4 drugs (INH 300mg + Rifampicin 600mg + Emb 800mg + PZA 1500mg OD) and two drugs regimen (INH 300mg + Rmp 600mg OD) for 10 months.

Repeat CSF analysis after 2 weeks revealed no cells with normal protein and sugar. Patient showed clinical improvement in her headache and vision but amenorrhoea galactorrhoea continued and patient did not conceive.

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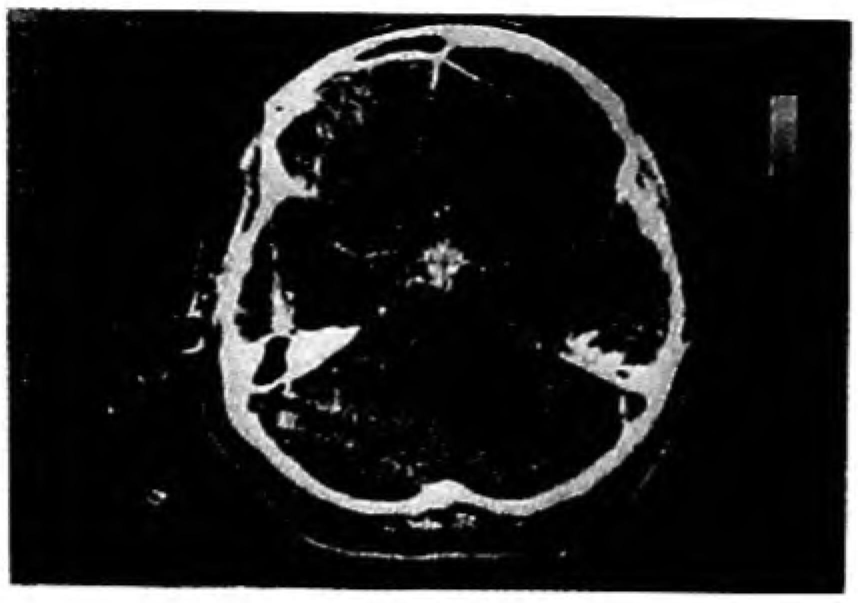
Patient underwent gyneacological checkup which was normal. Both secondary infertility and amenorrhoea were attributed to hyperprolactinemic state and patient was put on Bromocriptine 5mg OD. Patient restarted her menstrual cycle after 6 months of this treatment and later on conceived and is now pregnant for last 28 weeks.



CT Brain showing multiple isodense lesions in mid brain and supra seller region

Discussion

A tuberculoma of the brain forms when intracranial tubercles enlarge without rupturing into the subarachnoid space, walled off from the brain parenchyma by a thick fibrous capsule, these structures may reach considerable size before symptoms result. Tuberculomas may occur simultaneously with tuberculous meningitis or more often independently. They are also known to occur or enlarge to detectable proportions - during a course of therapy for tuberculous meningitis, presumably as a consequence of the inflammatory response to antigen released during treatment. No age, sex, racial or other factor has been identified to predict whether central nervous system tuberculosis will manifest as meningitis or as a mass lesion.

In the absence of concomitant meningitis, the symptoms of tuberculoma are those of single or multiple intracranial masses. Most patients have single lesions although as many as 12 have been identified within a single cranium (1,2) they have been reported throughout the cerebral hemisphere, basal ganglia, brain stem, cerebellum as well as substance of the spinal cord (3-5). Tuberculomas remain among the most common intracranial mass lesion in developing countries but are now thought to be rare in the western world (6,7). However, the increased availability of CT and MRI scanning has undoubtedly resulted in a greater recognition of these lesions in all contexts.

Symptoms are often limited to seizures. Fever and systemic toxicity are rare (8,9). The protein content of the CSF may be elevated but other abnormalities in CSF are not usually reported (5). Endocrinopathies may become evident months or years after recovery from tuberculous meningitis. This is most likely due to progressive scarring of either the hypothalamus itself or adjacent basal cisterns. Obesity, hypogonadism, Frolich's syndrome, sexual precocity, diabetes insipidus, hyperprolactinemic state (due to stalk compression) and growth retardation have been reported. The commonest abnormality observed is obesity with hypogonadism at times presenting as picture of Frolich's syndrome[10-12] - Summers et al 1968[13] described a girl with amenorrhoea four years after tuberculous meningitis due to tuberculomas in suprasellar region (hyperprolactinemic state due to stalk section). Later on after 14 years it progressed to secondary hypothyroid and hypocortisol state.

The diagnosis of tuberculoma is primarily radiologic and pathologic. Angiogram shows an avascular mass, sometimes with a faint tumourblush and CT Scanning typically shows either uniform contrast enhancement or a thick rim of enhancement surrounding a punctuate central clearing representing the caseous center of the lesion. MRI Scanning with enhancement depicts similar findings and appears to be more sensitive than CT in the detection of these lesions[16,17].

A diagonsis of tuberculoma can be confirmed only by biopsy. The gold standard of diagnosis is demonstration of caseating granuloma in tissue pathology. AFB smears of tissue specimens are positive in only about 60 percent of cases, similar proportion of specimens grow mycobacteria in culture. Extensive surgical resection is rarely required for definitive treatment of this condition[18,19] In recent studies, patients with medical treatment alone have achieved better functional recovery than those whose lesions were surgically removed[10,21].

The patient discussed represents an unusual complication of CNS tuberculosis, hence it is stressed here that in a patient of endocrinopathy even with a minor clinical suspicion of tuberculosis, this treatable cause should be ruled out especially in developing countries where prevalence of tuberculosis is quite high.

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I Dr. G.M. Malik hereby declare that the particulars given above, are true to the best of my knowledge and belief.

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Dr. G.M. Malik

Scalp Favus in Elderly

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Abstract: *In Kashmir scalp favus is commonly seen in prepubertal individuals. Favus of elderly is very uncommon. We report a case of scalp favus in a 60 years old female.*

Key words: *Favus, Tinea capitis.*

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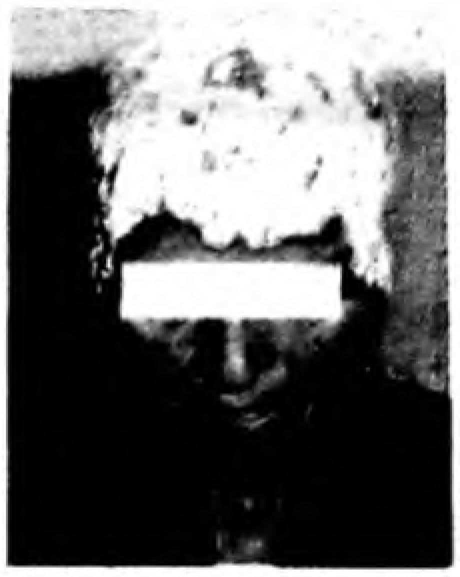
Case Report

A 60 year old female presented to us with crusted lesions with associated alopecia of scalp of 6 months duration. General physical examination revealed no significant findings, and systemic examination was normal. The local examination revealed extensive yellowish crusted lesions over whole scalp (Fig.I), which was associated with alopecia. No lymphadenopathy was present.



Routine investigations were normal. KOH test revealed mycelia, and the culture grew Trichophyton Schoeleinii. Diagnosis of favus was confirmed. Patient was put on oral grisofulvin, recovery was complete.

Discussion

Infection with T. schoenleinii is seen sporadically in different countries ranging from South Africa, the middle East, Pakistan, USA, UK, to Australia[1]. The classical picture of tinea capitis due to this organism is characterized by the presence of yellowish cup-shaped crusts known as scutula[2]. Each scutulum develops round a hair which pierces it centrally. Adjacent cursts coalesc to form a mass of yellow crusts. Extensive alopecia with atrophy interspersed among patches of the normal hair may be found in long standing cases. The various forms of tinea capitis including favus is very rare in post pubertal individuals. Our case was 60 year female showing classical features of favus. Favus of body has been reported by us previously[3].

Fungal infections of the skin are common irrespective of the age, scalp fungal infections are rare in post pubertal individuals. The factors responsible for this are not clearly under stood, widely accepted view is that sebum which increases in quantity after puberty has dermatophyte inhibitory properties. Fatty acids of sebum inhibit dermatophyte growth in vitro. This activity appear to reside in saturated fatty acids with chain length of 7,9,11, and 13 carbon residues. It was originally believed that the known tendency of M. andouni scalp ringworm to clear spontaneously at puberty was due to change in sebum compositions at this age, containing higher concentrations of these inhibitory fatty acids. However when it was established that composition of pre-and post pubertal sebum was in fact same the emphasis of the argument changed to increase in the total amount of sebum occuring at puberty. Serum factors also appear to be able to inhibit the growth of dermatophytes invitro and on cultured explants of skin. It is not entirely clear what is responsible for this, but unsaturated transferrins are known to inhibit the growth of dermatophytes by binding to the hyphae.

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Monitoring of Lithium Treatment

Since its introduction into psychiatry more than 40 years ago, lithium treatment has in most countries gained wide acceptance in the prophylaxis of unipolar and bipolar affective disorders. When lithium was first used for the treatment of mania by John Cade, he did not monitor the treatment through laboratory examinations. Doses were increased until side effects appeared and were then reduced somewhat for continued treatment. This procedure would hardly be considered good treatment practice today, when lithium determinations are rapid, accurate and the facilities for laboratory monitoring are available.

However, such conditions do not prevail everywhere. In developing countries, even strongly indicated lithium treatment is often not instituted because facilities for laboratory monitoring are un-available, and poor patients usually do not receive treatment with lithium, because they cannot afford the cost of regular laboratory examinations.

Clinical and laboratory monitoring of lithium treatment is important to maintain effective and safe therapy and to keep side-effects to a minimum. During the past years, there has been debate about the need for, and the frequency of routine serum lithium concentrations[1,2,3]. During lithium treatment, the serum lithium concentration may be determined once a week for the first 2-3 weeks, while dosage adjustment takes place. Thereafter, the patients may be followed with regular laboratory examinations at intervals of 1-6 months. The serum lithium concentration is determined in a blood sample drawn 12 hrs. after the last lithium intake and under steady-state conditions, i.e. atleast 4-5 days after the start of treatment and after dosage changes, and on the basis of this value, the dosage is adjusted to provide a serum concentration within the range 0.5-0.8 mEq/L.

Serum lithium values within the range 0.5-0.8 mEq/L are appropriate for most patients[4]. A few patients mostly among the elderly, do not tolerate and do not need concentration higher than 0.3-0.4 mEq/L. A few young patients may require levels of 0.9-1.0 mEq/L to derive full benefit from the treatment.

The Department of Clinical Pharmacology, SKIMS, Srinagar; is the only place in whole valley where the facility for estimation of lithium levels is available. Therefore, almost all the patients of manic depressive psychosis are being referred to this department through Hospital for Psychiatric Diseases, Srinagar or private clinics for monitoring of serum lithium levels. The effectiveness of lithium prophylaxis in more than 1000 patients of manic depressive psychosis was analysed in terms of dosage serum levels and renal function, over a period of 9 years and the pilot studies to this effect already stand reported[5,6,7]. In preventing recurrences of MDP, serum lithium levels ranging between 0.3 and 0.5 mEq/L and the doses below 750 mg/day, were found in-effective. The effective dosage in preventing recurrences were seen to be 750-900 mg/day with serum lithium levels between 0.6-0.9 mEq/L. However, serum lithium levels above 1.0 mEq/L and the doses above 1000 mg/day were associated with side-effects like fine hand tremors, dryness of mouth, thirst and weight gain.

At one time, it was feared that lithium treatment might lead to a decrease in glomercular filtration rate, but the investigation on renal function conducted in these patients revealed that even long-term treatment dose not lead to changes in glomerular filtration rate or to renal failures. The data indicate that the dosage regimen of lithium carbonate from 750-900 mg/day with serum lithium levels between 0.6 and 0.9 mEq/L is safe and provides effective prophylaxs, ensures good compliance and even long-term treatment does not induce renal insufficiency. During treatment, regular laboratory monitoring of serum lithium and creatinine concentrations is recommended. Recent studies suggest that long term lithium treatment does not raise the mortality of manic depressive patients and indeed may have a mortality lowering and antisuicidal effect. Despite the availability of alternative therapies, lithium remains the treatment of choice for the prophylaxis of recurrent manic depressive illness.

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Disseminated Candidiasis - An Emerging Nosocomial Infection

Riyaz Bashir MD,; Faroque A. Khan MACP

Once a rare disease disseminated candidiasis has become one of the most common nosocomial infection[1]. This secular trend is attributable to widespread use of antibiotics, immunosuppresive therapy and intensive care modalities. Candida is a yeast which constitute the normal flora of the mucocutaneous body surfaces, and is one of the most common causes of various superficial skin diseases and vulvovaginitis. They may however overgrow during states of impaired host defences and lead to an invasive and a life threatening disease.

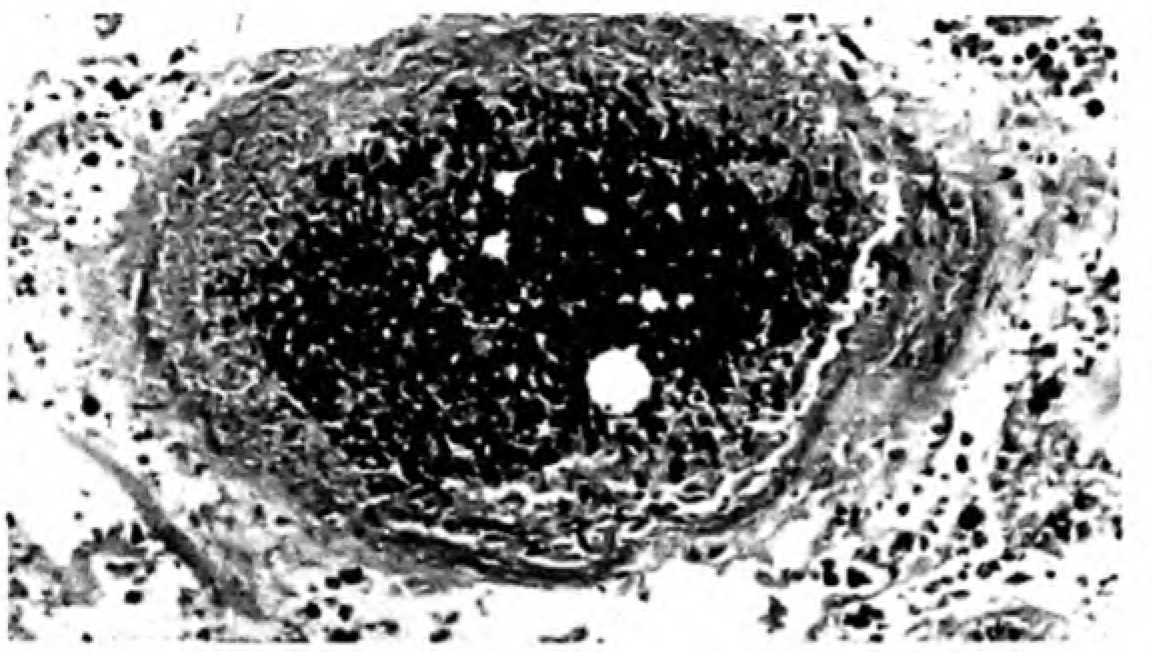

Fig I Special staining showing invasive candidiasis

Out of the many species causing infections in humans including C tropicalis, C. krusei, C. glabrata, C.albicans remains the most common cause of clinical infection. We present a case of disseminated candidiasis that typically highlights the risk factors and clinical course of this disease.

Case Report

A seventy three year old African American female with a past history of COPD was brought to Emergency room with shortness of breath for one day. She was intubated and admitted to our Intensive care unit with a diagnosis of Exacerbation of COPD. Her medications included Prednisone (30 mgms a day for a period of more than 8 months), Atrovent, Proventil, theophylline and home O_2 therapy. She was also taking Tegretol for her Trigeminal neuralgia. She was a smoker till one year ago. She denied any history of alcoholism or intravenous drug use. Her past surgical history was significant only for a hysterectomy 30 years ago.

She was started on Cefuroxime (Zinacef), Erythromycin and Solumedrol. She was also continued on her previous medications of Atrovent, Proventil, Tegretol and Oxygen.

On the third hospital day she developed loss of bowel sounds and radiographic studies indicated small intestinal obstruction which was managed conservatively with nasogastric suction, rectal tube, and TPN (Total parenteral nutrition). She was also noted to have a fever and an increasing white cell count. Despite conservative measures patient's condtion continued to deteriorate. On her ninth day in the hospital she underwent an explorative laparotomy, which revealed multiple adhesions for which adhesionolysis was done. Meanwhile blood culture results came positive for Staphylococcus epidermidis. Hence her antibiotics were changed to vancomycin, ceftazidime and flagyl. Postoperative course was marked by multiple unsuccessful attempts at weaning in our pulmonary care unit.

Patient responded initially to these antibiotics and was afebrile till day 23 of hospitalization. All through her course she received TPN and parental antibiotics. On day 24 she developed fever and was noted to have a erythematous pustular rash on her upper half of the back. The rash was treated with topical Lotrimin cream and antibiotics were empirically changed to Imipenem and Amikacin. Multiple blood cultures were done all of which were negative. Despite this treatment patient continued to be septic requiring vasopressors to support her blood pressure. At this time her chest roentgenogram revealed left lower lobe infiltrate, and blood glucose was greater than 400mg/dl. On day 30 she become severely hypotensive requiring multiple pressors and developed cardiac arrest from which she could not be resusscitated.

An autopsy was done which revealed multiple abscesses in the lungs, liver, spleen and kidney. The special staining of these abscesses reveal Candida albicans (Fig 1). Hence the cause of death was considered to be disseminated candidiasis.

Discussion

Every year about 120,000 patients in United States are affected by disseminated candidiasis[2,3].

The overall mortality of disseminated candidiasis has been estimated to be up to 50 percent. It consitutes about 15 percent of all hospital-acquired infections. Candida albicans, is the most common causative agent. Others being C.tropicalis, C.glabrata, C.parapsilosis and C.krusei.

The risk factors for disseminated candidiasis include use of *broad spectrum antibiotics, central venous and arterial catheters, hyperalimentation, neutropenia, post surgical patients particularly one's with abdominal surgery and with a protracted hospitalization, burns and transplant patients.* Our patient was on prolonged broad-spectrum antibiotics, needed central venous and arterial accesses, required hyperalimentation and abdominal surgery. According to Montgomery and Edwards 16% of patients receiving intravenous hyperalimentation develop disseminated candidiasis and possible mechanism, being hyperglycemia as was seen in our patient[4].

Disseminated candidates is an important cause of sepsis syndrome and multi-organ system failure. The other manifestations include a skin rash (Candida miliaria) and endophthalmitis. Patients with sepsis syndrome due to Candida present with chills, fever, hypotension and prostration. Multiple organs are usually involved in the form of diffuse microabcesses. Renal involvement is the most common. In Louria's series fo 22 patients 20 developed renal complications[5]. Involvement of the brain, lungs, spleen and liver reflects a major and often a preterminal breakdown in the host defense mechanisms. Myo~arditis also occurs frequently but premortem diagnosis is not so common. Our patient developed severe sepsis syndrome and septic shock despite on multiple antibiotics. Autopsy revealed multi-organ involvement in the form of diffuse microabscesses in the lungs, liver, spleen and kidneys.

Skin lesions in this condition represent embolic foci[6] but are seen in only a minority of patients and are 0.5-1 cm, pink or red, single or multiple and sometimes generalized lesions may appear. In our patient the skin scrapings on KOH testing showed Candida. These lesions are seen usually on the back and buttocks i.e. areas of pressure, as were seen in our patient.

Endophthalmitis is seen in 20-50% of patients with disseminated candidiasis, and correlates with multiple visceral involvement. Fundoscopic examination reveals white, cotton like circumscribed exudates with filamentous borders in chorioretina extending into the vitreous. Diagnosis of endophthalmitis at times requires serial fundoscopic eye examination, and when present is highly suggestive of disseminated candidiasis.

In the diagnosis of disseminated candidiasis, time is of great essence. The rate of premortem diagnosis is about 10-40 percent[7]. Blood cultures are negative in more than 50 percent of cases. The most important diagnostic technique in a high-risk patient is a thorough daily physical examination including *fundoscopy*. the definitive diagnosis can be made only by a histopathological demonstration of Candida from a normally sterile body sites. Skin tests are not useful and serological tests are not yet reliable enough. Hence presumptive clinical diagnosis is often a basis for initiating empiric antifungal therapy.

The mainstay in the treatment of disseminated candidiasis is systemic antifungal chemotherapy, treatment of the underlying illness, and changing all the lines including central venous catheters. Amphotericin B has a broad activity against various Candida species and has traditionally been the agent of choice in disseminated candidiasis. However, due to significant toxicity from this agent recently several studies have focussed on Fluconazole as an effective alternative. Randomized controlled trials comparing Fluconazole 400mgs/day with Amphotericin B in non-neutropenic patients with disseminated candidiasis have revealed similar outcomes for each drug[8]. However, it is recommended to use Amphotericin B (0.7mgs/kg/day) in patients with severe sepsis like illness, leukopenia and fluconazole resistant infection and continued for 2 weeks after signs and symptoms of infection have been resolved[9]. In their review Filler and Edward favor using Fluconazole as primary therapy only in those neutropenic patients who meet the following criteria: (!) clinically stable. (2) No evidence of hematogenous dissemination: (3) Candidemia in association with intravascular catheters: (4) Not receiving an Azole on a prophylactic basis: (5) Infections with aspergillus species are uncommon at that center[9]

Conclusion

- ✰ Disseminated candidiasis is an emerging nosocomial infection with very high mortality.
- ✰ High index of clinical suspicion is needed in the setting of risk factor i.e. use of broad spectrum antibiotics, central venous and arterial catheters, hyperalimentation, neutropenia, postsurgical and burns patients.
- ✰ Serial fundoscopic examination is a very important

bedside clinical tool that helps in the diagnosis of this condition.

- In patients with risk factors and physical findings, empiric therapy with antifungal agents should be started as soon as possible.

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Clinical Image

Staphylococcus Capitis Endocarditis

Abdullah Al-Rashdan MD, Riaz Bashir MD, Faroque A. Khan MACP.

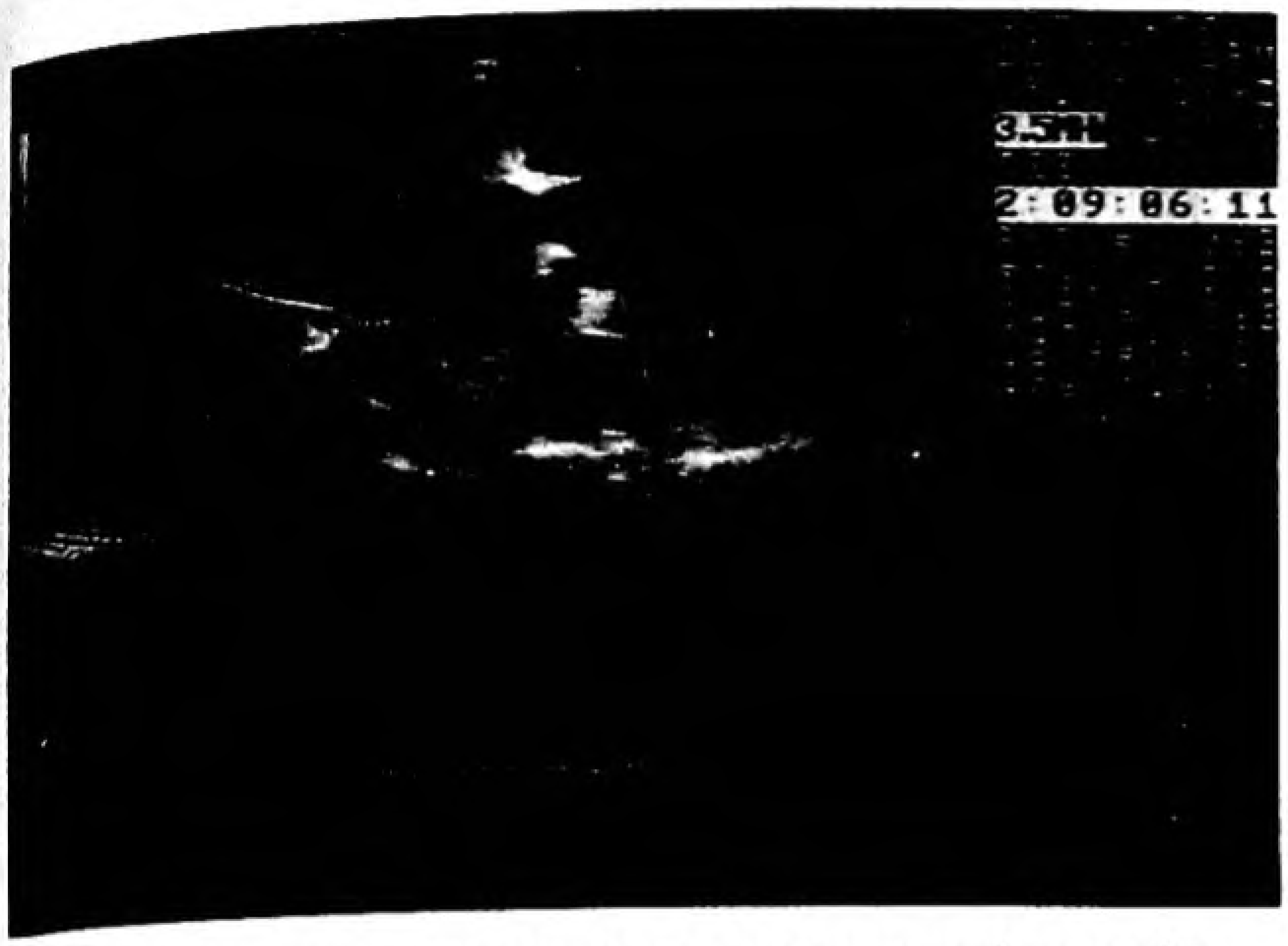

Fig. I Transthoracic echocardiogram showing stenosis and aortic valve vegetation

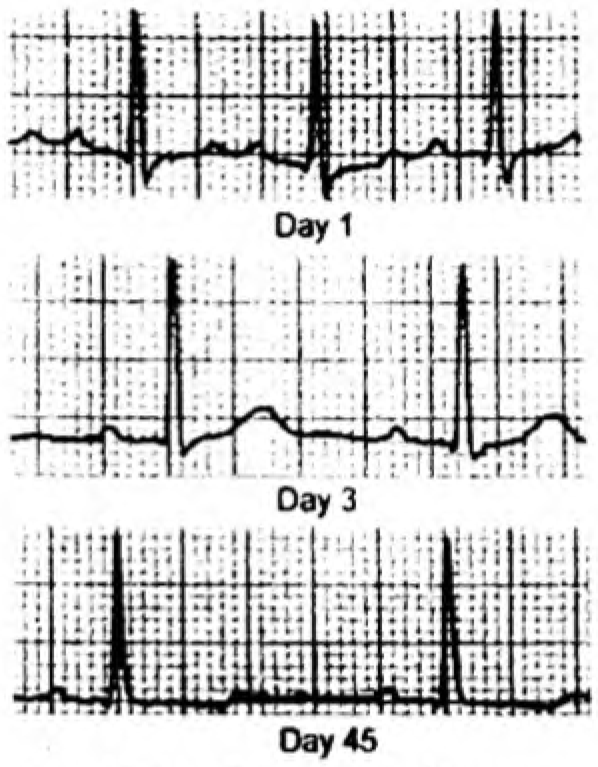

Fig. II Serial Electrocardiograms

A 70-year old white male with past history of aortic stenosis and NIDDM presented with complaints of fever and fatigue for two days. Denied any history of.chest pain, shortness of breath or any urinary symptoms. On physical examination patient had temperature of 104°F, pulse of 108 bpm and blood pressure of 150/80 mmHg. Cardiovascular exam revealed a grade III/VI systolic murmur in the aortic area. Rest of the physical examination including skin and scalp was unremarkable. Electrocardiogram showed sinus tachycardia with mild prolongation of PR interval. A transthoracic echocardiogram showed calcific aortic stenosis and 1 cm aortic valve vegetation on the aortic valve leaflet (Fig.1). Patient was started on antibiotics (Nafcillin and Gentamicin). Serial electrocardiograms demonstrated progressive prolongation of PR interval initially peaking at 224 milliseconds on day 3, later returning to normal (Fig.2). Three sets of blood cultures were positive for Staph capitis, identified by the DADE microscan using a positive break point combo panel. He completed six weeks of intravenous antibiotics with remarkable improvement. Staphylococcus capitis is a normal commensal of the skin, scalp and forehead. It is a gram positive, catalase positive, coagulase negative microorganism, closely related to staphylococcus epidermidis.

Our case illustrates that Staph capitis bacteremia should raise the suspicion of endocarditis, particularly in elderly patients who are prone to pre-existing aortic valve disease.

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Emergency Exposure to HIV

Mitchell H. Katz, MD, and Julie Louise Gerberding MD, MPH

Until recently, patients had little motivation to seek medical care soon after sexual exposure to HIV. However, evidence that antiretroviral treatment prevents HIV infection after occupational exposure has led to the recommendation that prophylaxis be considered after sexual exposure. This recommendation will result in an increased number of recently exposed patients presenting for care. Clinicians should seize this opportunity to reach persons who are at high risk for HIV seroconversion and provide them with evaluation, treatment, and counseling. A comprehensive approach to the care of persons recently exposed to HIV is proposed. Candidates for postexposure prophylaxis should be identified and given appropriate antiretroviral treatment. Physicians must perform HIV antibody testing to determinie which persons are already infected with HIV and must do baseline laboratory studies. Follow-up care includes assessment of side effects from postexposure treatment and surveillance for development of primary HIV infection. Most important, clinicians must ;provide risk-reduction counseling to decrease the chance of future exposures. Public health messages must emphasize that postexposure treatment should be used only as a backup for failure of primary prevention methods, such as avoidance of high-risk sexual exposures use of condoms.

Physicians in primary care settings, emergency departments, and sexually transmitted disease clinics must be prepared to evaluate, treat, and counsel patients with recent sexual exposure to HIV. Several tasks should be accomplished during the initial visit. First, appropriate candidates for postexposure prophylaxis should be identified and offered antiretroviral treatment. Second, HIV testing must be performed to identify persons who are already infected and need long-term, antiretroviral therapy. Finally, interventions to prevent future transmission of HIV must be initiated.

Rationale for Postexposure Treatment

The theory underlying the use of postexposure prophylaxis is that antiretroviral treatment instituted immediately after exposure to HIV may abort infection by inhibiting local HIV replication and allowing the host's immune defenses to eradicate the virus inoculum. Although no direct evidence shows that postexposure treatment prevents infection after sexual exposure, this is biologically plausible given the efficacy of treatment after transcutaneous occupational exposure and the similarities between the immune responses to transcutaneous and transmucosal exposures.

Identification of Candidates for Treatment

Identification of candidates for postexposure treatment requires assessment of the type of sexual exposure, the HIV status of the patient and the patient's partner, the patient's attitude toward safer sex, and the length of time since the exposure

Type of Sexual Exposure

Few studies have assessed the per-episode risk for HIV infection with specific sexual practices. The probability is highest with unprotected receptive anal intercouse (0.008 to 0.032). The risk is higher with receptive vaginal intercourse (.0005 to 0.0015) than with insertive vaginal intercourse (0.0003 to 0.0009). No per-contact estimates of risk with insertive anal intercourse or with oral intercourse have been published, although seroconversion as a result of oral sex has been documented.

Even for sexual acts for which the average per-exposure risk has been quantified, the average risk may not apply to a specific encounter. In some cases, HIV infections result from few contacts, in others, HIV infection does not occur despite many contacts. Many source and host factors influence the likelihood of HIV infection.

HIV Status of the Patient

Preventive treatment is given on the basis of the assumption that the patient is not already HIV infected. Many persons at risk have never been tested however, and others will have had unsafe sex since 6 months before their last negative test result. For these reasons, an HIV antibody test should be done during the initial visit. With conventional HIV assays, most infected persons will have detectable antibodies 4 to 6 weeks after exposure and almost all will seroconvert by 6 months. If the patient

JK-Practitioner 1998; 5(3):236-238
Source: Ann Int Med Vol 128 No 4 15(Feb) 1998; pp 306-12

reports having had multiple exposures in the recent past, and HIV viral load test should be performed to detect primary HIV infection. Testing for HIV should not prevent the immediate initiation of prophylaxis. Rapid HIV tests are extremely sensitive but are not specific enough to definitively diagnose pre-existing HIV infection. Patients found to be HIV infected at baseline should be prescribed an optimal drug regimen for primary or long-standing HIV infection.

Assessment of Sexual Partner (Source of Infection)

The HIV status of the sexual partner may not be known if he or she has never been tested or has engaged in unsafe behaviors since 6 months before the last negative test result. If the partner is willing to be tested, treatment can be started and then stopped if the partner's HIV antibody test result is negative. If the partner is unavailable or unwilling to be tested, treatment decisions should be based on the likelihood that the partner is HIV infected. Factors to consider include the partner's HIV risk behaviors and the prevalence of HIV and AIDS in the partner's community.

If the partner is HIV infected, additional information, including stage of illness and results of recent HIV viral load tests, can improve treatment decisions. Persons with advanced disease and high viral loads are more likely to transmit HIV. Because the correlation between plasma and genital fluid viral titer varies transmission may still occur even if the source has a nondetectable serum viral load. A history of antiretroviral treatment can identify cases in which drug resistance is more likely so that the prophylactic regimen can be adjusted. Care of the source patient should include counseling on how future risks can be avoided, both with the partner who has presented for care and with other partners.

Several probable cases of HIV transmission during rape have been reported and postexposure prophylaxis of HIV infection should always be considered and recommended when it is indicated.

Patient Attitude toward Safer Sex

Many motivated persons diligently practice safer sex but are accidentally exposed to HIV when a condom breaks. Reported per-episode failure rates with condoms are high (0.9% to 4.5%). In contrast, some persons may seek postexposure prophylxis in the hope that it will enable them to maintain high-risk behaviors without being infected.

Between these two extremes, patients present with various risk histories. Some have an isolated episode of unsafe sex while high on substances. Others may have many unsafe exposures with partners of unknown HIV status but seek care because of exposure to HIV through a partner who is known to be infected. Because it is difficult to assess a patient's motivation for practicing safer sex in the short time frame necessary to initiate postexposure treatment, clinicians should err on the side of offering treatment for an exposure but should emphasize the importance of safer sexual behavior in the future.

Recommendations for Postexposure Prophylaxis

We recommend postexposure prophylaxis after unprotected receptive and insertive anal and vaginal intercourse with a partner who is or is likely to be HIV infected (Table 1). Prophylaxis should also be offered for receptive fellatio with ejaculation, although the lack of per-contact estimate for this behaviour makes it more difficult to weigh the benefits against the risks. We do not recommend prophylaxis after other sexual exposures, such as cunnilingus or receptive fellatio without ejaculation, unless factors are present that increase the likelihood of transmission (such as exposure to menstrual blood). We recommend treating only isolated exposures or exposures in a patient who is willing to practice safer behaviors in the future. Finally, immediate treatment is optimal, and treatment should be initiated within 72 hours (the cut-off suggested for occupational exposures).

Table 1 Recommendations for Postexposure Prophylaxis

postexposure prophylaxis is recommended if

- The HIV exposure is high risk, specifically
  - Unprotected receptive anal intercourse
  - Unprotected receptive vaginal intercouse
  - Unprotected insertive vaginal intercouse
  - Unprotected insertive anal intercouse
  - Unprotected receptive fellatio with ejaculation
- The patient's partner is known to be HIV infected or is in an HIV risk group (such as gay or bisexual men, injection drug users, or sex workers).
- The exposure is isolated or the patient has made a commitment to safer sex in the future.
- The exposure occurred within 72 hours of presentation for care.

Table 2 Treatment Protocol for Postexposure Prophylaxis

Treatment regimen (4 weeks)
  Zidovudine, 200 mg orally three times a day or 300 mg orally twice a day. Lamivudine, 150 mg orally twice a day
Alternative regimen
  Stauvdine, 40 mg orally twice a day
  Didanosine, 200 mg orally twice a day (if patient weighs > 60kg) or 125 mg orally twice a day (if patient weighs <60kg)
With either regimen
  Consider adding a protease inhibitor (nelfinavir, 750 mg orally every 8 hours with meals, or indinavir, 800 mg every 8 hours on an empty stomach if source partner has a high viral load (> 50,000 copies/ml), has advanced HIV disease, or has been previously treated with one or both of the nucleoside analogues in the recommended two-drug regimens
  Offer emergency contraception to women who did not use contraception
Testing of exposed patient
  HIV antibody test
  HIV viral load count (if patient has had several episodes of unsafe sex in the past 6 months)
  Hepatitis B virus antibody test
  Hepatitis C virus antibody test
  Gonorrhea, syphilis, and chlamydial tests
  Pregnancy test (if appropriate)
Baseline laboratory tests for postexposure prophylaxis
  Complete blood count
  Liver function tests
  Renal function tests

Peptic Ulcer Disease-Antral Gastritis & H Pylori (Significant Correlation)

This study was undertaken to find the association of Helicobacter pylori infection with chronic antral gastritis in peptic ulcer disease patients and healthy population of Kashmir.

50 peptic ulcer patients (duodenal ulcer=46, gastric ulcer=2 and combined duodenal and gastric ulcer=2) and 30 asymptomatic healthy volunteers were included in this study. Peptic ulcer was diagnosed on endoscopic examination, 4-6 punch biopsies were taken from gastric antrum in all the individuals and in case of gastric ulcer an additional biopsy was taken from the edge of the ulcer to exclude its malignant nature. Helicobacter pylori (H. pylori) organism was diagnosed using three different test methods, viz. Histology (using Giemsa Stain), Microbiology (Gram Stain) and Biochemistry (using One minute Endosocpy Room Test). Histological diagnosis of H. pylori was taken as the "gold standard" for the presence of H. pylori organism. Histological diagnosis of gastritis was made using Hematoxylin and Eosin Stain and the gastritis was classified as active chronic gastritis and superficial chronic gastritis.

Out of 30 peptic ulcer disease patients with associated antral gastritis, 27 (90%) were positive for H. pylori on histological examination (13 superficial chronic gastirtis and 14 active chronic gastritis) whereas out of 8 healthy volunteers with histological evidence of chronic antral gastritis, H.pylori was observed in 7 individuals (87.50%) (4 active chronic gastritis and 3 superficial chronic gastritis).

A highly significant association between H. pylori infection with chronic antral gastritis both in peptic ulcer disease patients and healthy volunteers of Kashmir was found in this study. Association between H.pylori infection and chronic gastritis was 90% in peptic ulcer group and 87.50% in healthy population ($P<0.005$).

Source:- *Romshoo GJ., Malik G.M., Bhat MY., Rather et al. Helicobactor Pylori Associated Antral Gastritis in Peptic Ulcer Disease Patients and Normal Healthy Population of Kashmir, India. Diagnostic and Therapeutic Endoscopy. 1998; 1:135-39.*

Organophosphorus Poisoning in the Kashmir Valley, 1994 to 1997

We prospectively studied 164 patients (age range, 14 to 58 years) from different districts of the Kashmir valley, who were seen in the casualty department of SMHS Hospital, Srinagar, India, with a history of exposure to organophosphors compounds between April 1994 and July 1997, Most of the patients (74.4 percent) had consumed these agents to attempt suicide. Phosphamidon was the agent most frequently ingested Two thirds of the patients lived in districts with large areas of apple orchards. About 90 percent had consumed 5 to 50 ml of various agents; the rest had taken more. About 80 percent were seen within two to four hours. Thirty-eight patients (23.2 percent) initially denied consumption of these agents, though they had clinical features of poisoning. The precipitation factors in the suicide attempts were strained social relations (in 30.3 percent, mainly caused by the death of a close relative in the current political unrest), failure in examinations (20.5 percent), unemployment (18.0 percent), failure in love affairs (14.0 percent), and others (17.1 percent). Nine patients died, and 155 recovered.

Organophosphorus compounds are commonly used as inseciticides, pesticides, and fungicides in Kashmir. Since 1990, political unrest has caused great suffering and mental trauma among the residents of Kashmir. The high ineidence of organophosphorus poisoning with suicidal intent is but one of many manifestations of the tragic consequences of this unrest.

Sources: *Malik G.M.; Mubarik M.; Romshoo G.J. Organophosphorus Poisoning in the Kashmir Valley, 1994 to 1997. N Engl J Med. 1998 (April); 1078*

Pulled Elbow-Effect on Hypermobility of Joints

It is commonly stated that children who suffer with pulled elbow possess generalized increase in joint laxity, and indeed, at least one large series in the literature purports to demonstrate this. The authors of this paper examined 200 children with pulled elbow on a prospective basis, assessing them in particular for signs of hypermobility. The overall incidence of joint hypermobility in this group was found to be 8.5%. Those children who had experienced more than one episode were no more likely to be jointlax than the others. In a control group of 100 normal children, 10% exhibited hypermobility. It is clear from these results that joint hypermobility is not primarily responsible for this injury, and the authors suggest that various anatomical variations may have more to do with the aetiology.

Source: *Hagroo GA, Zaki HM, Choudhary MT, et al. Injury 1996; 26:687-90*

Cyclosporin and its Usefulness in Refractory Childhood Asthma

The Department of Paediatric Respiratory Medicine, Royal Brompton Hospital, London, assesses the use of cyclosporin in childhood corticosteroid dependent asthma. They suggest that cyclosporin mainly acts by inhibition of T helper lymphocyte function and has been seen to improve lung function.

The authors included 5 children with severe asthma who required atleast 10 mg of prednisolone daily in the study. These children were treated with cyclosporin over a period of eighteen months. The dose was titrated to maintain blood concentrations of 80-150 mg/L. In the course of the study, the authors were able to wean three children from prednisolone, but found that one quickly replapsed. One child failed to respond while in the other child the dose of steroid could be lowered. But in the latter unacceptable hirsutism was found to be an adverse effect. But none of the patients had any rise in creatinine, potassium or blood pressure over the baseline. It was also seen that irreversible renal damage was not found in any of the patients in this trial. But once the treatment was stopped, the usefulness of the treatment was found to be lost. The authors thus conclude that probably a very low dose of cyclosporin over a long term or even an inhaled/nebulised preparation may benefit the children. They suggest a controlled, multicentre trial to establish the benefit of this treatment.

M E Coren, M Rosenthal, A Bush. "The use of cyclosporin in corticosteroid dependent asthma". Archives of disease in childhood; Volume 77, 1997; page 522-523.

Analgesics and Ovarian Cancer have an Inverse Association

The. Department of Obstetrics and Gynecology, Harvard Medical School, Boston, USA, investigated the association between use of aspirin and other over the counter analgesics and their risk of ovarian cancer. The interest stemmed from the fact that these drugs reduce the risk for colorectal cancer.

The case control study compared the use of over the counter analgesics in 563 women who had ovarian cancer with 563 women from the general population. The exposure odds ratios were estimated. The use of these drugs was assessed through interviews as used atleast once a week continuously for atleast six months.

The authors found that the odds ratio for risk of ovarian cancer for aspirin use was 0.75, ibuprofen was 1.03 and that for paracetamol was 0.52, after all the adjustments were made for other factors like age, education, parity, religion, oral contraceptive use, menstrual, arthritis and headache.

It was seen that relative to no use, the lower risk for ovarian cancer is associated with paracetamol was more apparent for use on a daily basis, for more than 10 years of use or for more than 20 tablet years.

The authors thus conclude that in their study, there was a statistically significant inverse association between paracetamol use and ovarian cancer risk. There was no association with ibuprofen use but a modest association with aspirin use. The authors suggest that until the validity of an mechanism for the association between paracetamol and ovarian cancer protection are well defined, the association cannot promote a public health recommendation.

Daniel W Cramer, Bernard L Harlow, Linda Titus Ernstoff, Kari Bohike, Will.iam R Welch, E Robert Greenberg. "Over-the-counter analgesics and risk of ovarian cancer"; Volume 351, January 1998; pages 104-107.

The Female Condom

The article deals with the studies conducted on the female condom and summarises the selected acceptability studies in many other countries. The female condom according to the authors is made from polyurethane plastic with a ring made from the same material at either end. First marketed in 1992 in Switzerland, the authors report its availability in 13 countries as of 1996.

They report that a sixty country survey by UNAIDS estimated the global demand for female condoms at 134 million for 1998. Among perfect users the six month failure rate dropped over threefold, to 4.3% and the discontinuation rates were 55% for Latin Amercian women and 32% for the US women.

The article also details the statistics for the prevention of infection like trichomoniasis in the population. The usefulness of the product from a study of female sex workers in Thialand also supports the reduction of sexually transmitted diseases.

The acceptibility rates of the female are very high among both the sexes. the difficulties encountered are the difficulties with insertion, inner ring causing pain for both partners, and a few others. The acceptibility of the method lies in the provision of women with a barrier method they did not have to negotiate with their partner.

The article then goes on to detail the issues of availability and costs of the product in all the countries of its use. The authors stress that given that the men's cooperation is useful in its use, promoting the female to both male and female population is essential.

Product News. "The female condom: For men and Women"; Outlook; Vol. 15, 4, Dec. 1997; pages 4-6.

Tiagabine-a drug profile

This is a contribution from the University Department of Medicine and Therapeutics. Glasgow, UK. The authors report that the annual incidence of epilepsy in most developed countries is 50-70 per 1000000 individuals. In this context they go on to discuss tiagabine which is the first gama-aminobutyric acid (GABA) uptake inhibitor to be introduced into clinical practice. They stress that the manipulation of the GAB Aergic system is the recognised method of producing anticonvulsant activity.

They then go to the discuss the molecular details in the mechanism of action of the drug and the clinical pharmacokinetics. Tiagabine hydrochloride attains maximum concentration 90 minutes after ingestion of the drug. The hepatic metabolism of the drug is extensive and children are seen to eliminate the drug faster than adults. Using the data from the five double-blind placebo-controlled studies which reported on Tiagabine's efficacy as adjunctive therapy, the authors report that there was a significant reduction in simple and complex partial seizure frequency after using the drug. The article then elaborates upon the drug interactions and suggest that studies have failed to demonstate any clinically relevant interactions between tiagabine and cimetidine, theophylline, warfarin, digoxin, triazolam or oral contraceptive pill components.

To conclude, the authors describe the clinical use of the drug with an initial dosing in adults being 4-5 mg twice daily with weekly increments of 4-12mg. With this the therapeutic potential of the drug is discussed.

Source: Leach JP, Brodie MJ. "Tiagabine"; the Lancet; Volume 351, January 1998;p pages 203-207.

Screening of Tamoxifen Users - who and when?

This is a report on the debate by the Flemish Gynaecological Oncology group and the gynaecologists at the Algemene Kliniek St-Jan, Brussels on the effects of Tamoxifen and newer antioestrogens on the uterus.

The issue under debate was whether or not to screen the symptom free females taking Tamoxifen in an attempt to pick up endometrial lesions. The authors feel that Tamoxifen intake and endometrial carcinoma is related to total dose and duration of intake. The risk may be related to past oestrogen therapy and obesity.

Although reports suggest that DNA adducts formations are seen in experimental models, human endometrial do not reflect DNA adducts. The authors also suggest that the cytogenetic changes in endometrial polyps and DNA content in endometrial cancers from Tamoxifen treatment patients are the same as in non-users. The benefit of Tamoxifen as adjuvant treatment in recurrent endometrial cancer is stressed. The role of selective estrogen receptor modulators (pure and new generation antioestrogens) have a less proliferative effect on endometrial as compared to Tamoxifen, but their protective effect against carcinoma breast is debatable. The usefulness of endometrial screening by using repeatbiopsies or transvaginal ultrasound is suspect since most of the endometrial lesions due to the use of Tamoxifen are benign polyps. The finding of a thin endometrial strip of 5mm or less has a better predictive value for a normal uterine cavity.

The authors summarise that symptom free women can be screened annually with transvaginal ultrasonogram from 2-3 years after the start of Tamoxifen. Whether taking Tamoxifen for more than five years improves breast cancer survival is suspect, and the risks must be weighed against benefits.

Source: Neven Patrick, Vergote Ignace. "Should tamoxifen users be screened for endometrial lesions"; The Lancet; Volume 351, January 1998; page 155.

Defining the Needs of Children born to HIV Positive Mothers

This is a study from the Edinburgh Sick Children's NHS Trust, Edinburgh, and the authors aim to ascertain the psychological, social and education needs of children who are born to HIV positive mothers.

92 women (90 white) of whom 46 also had hepatitis C virus infection were included in the study. Mean age at delivery ws 25.6 years. 120 children born of these women were followed up for 58 months. 16 children were infected with HIV, 15 were of indeterminate status and 89 were uninfected. The authors report that 68% were cared for by their birth mother of whom 52% were single, 23 known to have symptomatic HIV disease. 25 mothers of 32 children had died with the mean age of the child at maternal death being 66.9 months. It was found that more infected than uninfected children knew of their mothers' condition (31% versus 5%). It was also seen that a larger proportion of the infected children had special educational needs (69% versus 13%). Only 28% were not receiving any support from the voluntary or other agencies.

The authors summarise by proposing the model of chronic illness as the standard of care of these children. They stress that these children require dedicated resources and commitment from health, education and social work agencies and the voluntary sector.

Source : Mok Jacqueline, Cooper Sarah. "The needs of children whose mothers have HIV infection"; Archives of Disease in Childhood; Volume 77, 1997; pages 483-487.

ACE Inhibitor use can cause hypoglycemia in Diabeties

To examine whether an association exists between the use of angiotensin-coverting enzyme (ACE) inhibitors and hospitalization for severe hypoglycemia in patients with diabetes mellitus.

6649 patients with diabetes who used insulin or oral antidiabetic drugs were identified using the DARTS database. 64 patients (median age 60 y, 61% men) who were hospitalized with severe hypoglycemia were studied as case-patients. Exclusion criteria were a hospital stay within 1 months of admission for hypoglycemia or abuse of antidiabetic drugs. Each patients was matched for sex and age with up to 7 control-patients. The control group consisted of 440 persons from the community.

Previous exposure to ACE inhibitors, B-blockers, and calcium antagonists; dose, strength, and type of diabetes treament; hemoglobin A_{1c} level; serum creatinine level; place of diabetes care; cardiovascular drug use; loop diuretic use (as a marker of heart failure); and duration of diabetes were taken as assessment of risk factors.

Use of ACE inhibitors was reported by 7 patients (11%) who where hospitalized for hypoglycemia and by 19 control patients (4%) ($P = 0.023$); the unadjusted odds ratio (OR) for hospitalization for hypoglycemia was 3.2 (95% CI 1.2 to 8.3). Use of B-blockers (OR 0.9, CI 0.3 to 3.3) and calcium antagonists (OR 1.7, CI 0.2 to 2.1) did not contribute to an increased risk for hospitalization. When the OR was adjusted for type of diabetes treatment, place of diabetes care, diuretic use, and duration of diabetes, the risk for hospitalization of patients using ACE inhibitors remained (OR 4.3, CI 1.2 to 16.0). Hypoglycemic patients were more likely than control-patients to have been insulin users, to have received hospital-based diabetes care or loop diuretics, and to have had a longer duration of diabetes. To conclude that ACE inhibitors had an increased risk for hospitalizarion resulting from severe hypoglycemia.

Source:- Morris AD, Boyle DI, McMahon AD, et al., and the DARTS/ME/MO Collaboration. ACE inhibitor use is associatedwith hospitalizationfor severe hypoglycemia in patients with diabetes. Diabetes Care. 1997 Sep; 20:1363-7.

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1. Basal laminae are interposed between epithelia and subepithelial conective tissue except in iris where the iris is separated from the posterior chamber by a thin basal lamina and thus, this limiting membrane is not bordered by connective tissue.
2. All the cells in cerebellum are inhibitory except granular cells.
3. All the nerve fibres are convered by endoneurieum except optic nerve fibres where these fibres are surrounded by the neuroglia (Astrocytes called as lemnocytes around optic nerve fibres near optic disc.)
4. All the muscles develop from mesoderm except iris and errector pilori.
5. Cells are nucleated except red blood cells (Adult) and platelets.
6. After Meiosis II the daughter cells are of unequal size except male germ cells.
7. All the cells divide except Neurons.
8. The size of the cells varies between 5 to 50 microns except ovum and large ganglion cells which attain the size of upto 130 to 150 microns.
9. The layout of epithelium is a simple or stratified covering all the free surfaces except in ovary, anterior lobe of pituitary and liver lobules where the epithelium forms solid cords.
10. Eipthelial cells are separated by scanty intercellular substance except in stratum corneum, alimentary canal (lining cells) and chorion where its existance is doubtful.
11. From nose to the terminal bronchiole the respiratory passage is lined by pseudostratified ciliated columnar epithelium except over vocal cords where the lining epithelium is stratified squamous (NK).
12. Granular endoplasmic reticulum is present in all the cells except in matured red blood cells.
13. Nucleoli stain one colour only except in Sertoli cells where the nucleolus is acidophilic centrally and basophilic peripherally.
14. The septae of gland may contain smooth muscle except bulbourethral gland where both the smooth as well as skeletal muscle is present in the septae of the glands.
15. Lysozyme is present in all the cells except Red blood cells.
16. Craniospinal ganglia have pseudounipolar neurons except spiral ganglion where the neurons are bipolar.
17. Mast cells present in the vicinity of blood vessels except those of central nervous system. (Mast cells are present in meningeal blood vessels. These cells are absent in spleen but numerous in thymus).
18. All the glands of the body have the architectural pattern analogus with a tree except kidney and liver.
19. During third week of development mesoderm spreads everywhere between ectoderm and endoderm except at the sites of the buccopharyngeal and cloacal membranes.
20. Veins are covered by smooth muscle/collagen except diploic veins which consist of endothelium covered by elastic fibres.
21. The veins drain by joining to form larger veins or continue as the veins/sinuses of larger calibre except cavernous sinus which divides into two divisions (Superio and inferior petrosal sinuses) of smaller calibres.
22. The arteries pass by the side of veins usually as medium sized arteries except internal carotid artery which (Covered by internal carotid nerve-sympathetic nerves) traverses almost through the lumen of the cavernous sinus (Separated by endothelium only from the lumen)
23. Nerves are supplied by adjoining arteries except central artery of the retina which also traverses some course within the optic nerve to its destination to the retina.
24. Venae nervi hypoglossi are the only veins which accompany a nerve hypoglossal nerves.
25. Synovial joints are covered by hyaline cartilage except the temporo mandibular joints where the articular surfaces are covered by the fibrous tissue. (The head of the mandible is covered by some hyaline cartilage.
26. Temporomandibular joints are an exception in that these develope from a membrane.
27. All bilateral joints may move individually or simultaneously except temporomandibuler joints which cannot move individually as the convex second surface of both the joints is formed by the same bone i.e. mandible.
28. Ansa cervicalis supplies all the infrahyoid muscles except thyrohyoid.
29. Longissimus cervicis is inserted into the transverse processes of all the cervical vertebrae except atlas.
30. Gap cell junctions are widely present except in skeletal muscles and the blood vessels.
31. Posterior interocostal arteries anastomose with the anterior intercostal arteries except the third posterior which anastomoses with the superior intercostal artery.
32. Adipose tissue is present everywhere in the body except subcutaneous tissue of the penis, scrotum,

eyelids, labia minora and cranial cavity.

33. In a symphysis the bones, their covering hyaline cartilage and the intervening fibrocartilage remain in close contact throughout the life and never fuse except symphysis and manubriosternal joints.
34. Exocrine glands have their lobules differentiated around the ductules except the liver where the lobules are differentiated around the venules. (Liver is the only exocrine gland of reticulate type).
35. Ducts divide in a dichotmous manner except the pancreas where the main duct remains throughout the length of pancrease to receive the tributyaries (Herring bone pattern).
36. Nerve fibres in central nervous system do not regenerate except supraopticohypophyseal tract.
37. The dendritic cells (Langerhan's cells) are present in epithelium except over tongue and cornea.
38. Hair grows in a slanting fashion everywhere in the body except over the lids where the eyelashes are vertical.
39. Sweat glands are present everywhere except lips, (Free margin), glands penis, nail beds and ear drums.
40. Sebaceous glands are present in association with hair except lips, glans penis and glans clitoridis.
41. Spinal ganglia lie in the intervertebral formina except sacral and coccygeal which lie in the sacral canal and the first two cervical which lie above and below the atlas.
42. All the descending tracts in the lateral funiculus of the spinal cord are crossed except olivospinal and the lateral vestibulospinal.
43. The lymph vessls traverse the lymph nodes before these drain in the the thoracic duct or the right lymphatic duct except oesophageal, thyroid, coronary, and the triangular ligament of the liver.
44. Azygos vein collects venous blood from the posterior intercostal spaces except the first.
45. Lower inguinal lymph nodes drain the whole lower limb except the area of the back and the lateral part of the calf.
46. Muscles arise at one site and get inserted at the other site except the orbital part of orbicularis oculi which has the same site of origin and insertion.
47. Glandular cells have no cilia except epithelial cells of efferent ductules of testes and the follicular cells of the thyroid gland.
48. The epithelial coverings are avascular all over the body except stria vascularis (On the lateral wall of cochlear duct-scala media) where intra epthelia capillary plexus is present between the supreficial (Chromophil) epithelial layer and the deeper light (Chromophobe) layer and the basal layers of epthelium and processes from all the cells of these layers extend to cover these capillaries.
49. The peri-osteum is uniform everywhere except over osseous spiral lamina where it is thickened and named as Limbus spiralis.
50. The bones are covered with periosteum which is subjacent to other periosseous tissues except mucous membrane which covers the periosteum of the auditory ossicles (Middle ear contains Malleus, Incus and Stapes which are the bones within/from the part of middle ear contents.
51. Stratified epithelial cells are usually nonsecretory and protective only except the cells of stria vascularis where major portion of the endolymph is secreted by these cells.
52. There is no overlap of nerves of either side across the midline of the body except over lips.
53. Sensory nerve endings are not visible to the naked eye except Pacinian corpuscles.
54. All the glands pour out their secretions either by mesocrine or apocrine or holocrine mode except mammary gland where the mode of secretion is both aprocrine as well as eccrine. (This means we are fed by the portions of the cells of our mothers which virtually means that our mothers feed us with their flesh in physical sense. How much indebted to our mothers we should be?)

From: ***Dr. Abdul Ahad,***
Associate Professor of Anatomy, Govt. Medical College Srinagar.

JK Practitioner 1998;5(3) 243-244

ECFMG Programmes

Exchange Visitor Sponsorship Program

The Educational Commission for Foreign Medical Graduates is authorized by the United States Information Agency (USIA) to sponsor foreign national physicians as Exchange Visitors in the United States. Participation is designated by visa sponsorship category of eigher J-1 Alien Physican (ACGME-accredited clinical training programs) or J-1 Research Scholar (short-term advanced research programs involving ovservation, consultation, teaching or research). After establishing an applicant's eligibility, ECFMG issues a Certificate of Eligibility for Exchange J-1 Status (From IAP-66).

The objectives of the Exchange Visitor Sponsorship Program are to enhance international exchange in the field of medicine and to promote mutual understanding between the people of the United States and other countries through the interchange of persons, knowledge and skills. ECFMG administers the Program in accordance with the provisions set forth in a Memorandum of Understanding between ECFMG and the USA and the Federal Regulations established to implement the Mutual Educational and Cultural Exchange Act. ECFMG is responsible to ensure that all Exchange Visitors and host institutions meet the federal requirements for participation.

The following table shows the number of Exchyange Visitors sponsored by ECFMG in accredited programs of graduate medical education and training in the United States for the academic year July 1, 1995 to June 30, 1996. The largest number of Exchange Visitors sponsored by ECFMG continue to be from India (19%), Pakistan (16%), and the Philippines (12%).

Program	**Count**
Allergy and Immunology	11
Anesthesiology	357
Colon and Rectal Surgery	6
Dermatology	24
Diagnostic Radiology	157
Emergency Medicine	36
Family Practice	251
General Surgery	574
Internal Medicine	5,628
Internal Medicine/Emergency Medicine	1
Internal Medicine/Neurology	3
Internal Medicine/Pediatrics	69
Internal Medicine/Psychiatry	4
Medical Genetics	14
Neurology	426
Neurosurgery	52
Nuclear Medicine	41
Obstetrics and Gynecology	107
Ophthalmology	102
Orthopeidc Surgery	72
Otolaryngology	385
Pediatrics	1,786
Pediatrics/Psychiatry/Child Psychiatry	2
Physical Medicine and rehabilitation	44
Plastic Surgery	25
Preventive Medicine	16
Psychiatry	622
Radiation Oncology	23
Thoracic Surgery	58
Transitional Training	72
Urology	33
Total	**11,026**

International Medical Scholars Program

The International Medical Scholars Program (IMSP) was formally established in 1988 by ECFMG for the purpose of assisting foreign physicians and others in health care leadership positions abroad to gain access to educational opportunities in the United States.

To date, fellowships have been awarded to 58 scholars from 34 countries. Forty-four U.S. medical institutions have servewd as hosts for the scholars.

Reports on the completed fellowships from both scholars and U.S. sponsors have consistently been very positive and indicate that IMSP is achieving its main objective of placing scholars in high-quality U.S. institutions that provide educational programs tailored to the specific needs of the scholars, their home country-sponsoring institutions, and their countries. A number of the fellowships have resulted in continuation and/or initiation of affiliations between the U.S. host institutions and the home country-sponsoring institutions.

For the 1996-97 IMSP program year, 146 applications were received and 84 were deemed eligible for review.

Foreign Faculty Fellowship Program in the Basic Medical Sciences

The Foreign Faculty Fellowship Program in the Basic Medical Sciences (FFFP), administered by ECFMG, enalbes selected teachers of the basic sciences from medical schools abroad to teach and study for a period

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Source: Educational Commission for Foreign Medical Graduates Annual Report 1996 ranging from six months to one academic year in a medical school in the United States. The programe was designed to enhance the teaching skills of basic science faculty in medical schools abroad and to strengthen the basic science departments in those schools.

Siunce the inception of the program in 1983, the Foreign Faculty Fellowship Program has awarded 152 fellowshps to individuals from 104 foreign medical schools in 52 countries. Sixty-eight U.S. medical schools have acted as host institutions for the Fellows. Following are the disciplines and the home country regions of the 152 awardees to date:

Disciplines

Physiology	47
Anatomy	42
Pharmacology	21
Biochemistry	17
Pathology	13
Microbiology	7
Immunology	2
Pathophysiology	1
Neuropatholoy	1
Cell Biology/genetics	1

Home Country Regions

East Asia/Pacific	37
Europe/Central Asia	23
Latin America/Caribbean	23
Middle East/North Africa	11
South Asia	24
Sub-Saharan Africa	34

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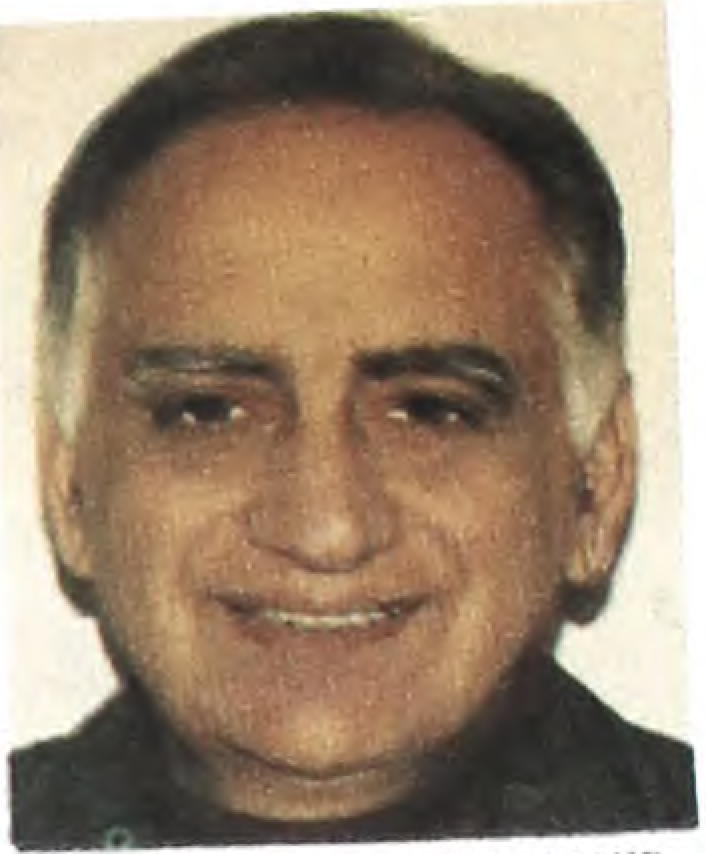
News

- **Dr. Faroque A Khan, MD**, Chairman Department of Medicine at Nassau County Medical Centre in East Meadow, N.Y; and Professor of Medicine at State University of New York (SUNY) at Stony Brook NY, was re-elected to the ACP Board of Regents. The announcement to this effect was made during the ACP's 79th annual session held April2-5, 1998 in San Diego.
  ACP is the country's largest medical specialty organization and has a membership of more than 100,000 internal medicine Physicians and medical students.
  An ACP fellow since 1978, Dr Khan has served as an ACP Regent since 1995. Regents serve a maximum of two three years term. Dr. Khan was named a Master of the American College of Physcians (MACP) in 1993, for his outstanding contributions to medicine.
  After earning his bachelors in medicine in Srinagar, Kashmir in 1964. Dr Khan did his residency training at Queens Hospital Centre in New York in 1967 and fellowship training in Pulmonology at Alber-Einstein College of Medicine in 1971. Recently Dr. Khan has been honoured as Laureate for 1998 by the New York Chapter of ACP abd New York Down state II Region of ACP for his outstanding contribution to medicine.



Dr. Faroque A Khan, MB; MACP

- **Dr. Syed Amin Tabish** (MD, MAMS, FIMSA, FRIPH), Asstt. Professor and Administrator, S.K. Institute of Medical Sciences represented India at The World Health Forum 1998 held at Dallas (Taxas), USA. The purpose was to examine Emerging and Re-emerging Infectius Diseases from an international perspective and to develop a set of guidelines for proactively managing, potential and recurring infectious diseases.
  Dr. Tabish's abridged biography has appeared in Marqui's Who's Who of the world 1998, USA. His biographical note has also appeared in Indo-European Who's Who, Indo-American Who's Who and Refernce Asia (Men of Achievement).

Conference Clander

- **VII National Neurotrauma Conference at Indore** from August 21 to 23, 1998. Contact: Dr VG Dakwale, Department of Neurosurgery, Choithram Hospital, Manik Bagh Road, Indore. Tel: (91) 0731-49165/65252/433410/62491-98. Fax: (91) 0731-470068, 537277.
- **National CME Programme on Frontiers of Internal Medicine at All India Institute of Medical Sciences**, New Delhi, in October, 1998. Contact: Dr Anoop Misra, Additional Professor, Deptt. of Medicine, All India Institute of Medical Sciences, New Delhi 110029. Tel: 6864851, Extn. 3571. Fax: 91-11 -6862663, e-mail: amisra@ medinst. emet. in.
- **XIIIth National Conference of Research Society of Anaesthesiology & Clinical Pharmacology** (RSACP) at Udaipur (Rajasthan) from October 10 to 12, 1998. Contact: Prof. (Miss) Pramila Bajaj, Organising Secretary, XIIIth National Conference of Research Society of Anaesthsiology and Clinical Pharmacology, 25, Polo Ground, Udaipur - 313001. Tel: (O) 0294-52811-17, Ext. 3279, (R) 0294-560 495.
- **5th Biennial Congress of Asian** and oceanic Society of regional Anaesthesia (AOSRA) at New Delhi from October 29 to November 2, 1999. Contact: Organizing Secretary, Room No. 5020, Deptt. Of Anaesthesiology & Intensive Care, All India Institute of Medical Science, Ansari Nagar, New Delhi - 110029. Tel: 91-11-685 9224, 659 3212; Fax: 91-11-686 2663.
- **4th World Congress & XIIth Indian Conference on Family Welfare & Voluntary Sterilization at Calcutta** from Novembber 20 to 22, 1998. Contact: Dr C S Dawn, 25-B, C.I.T Road, Calcutta-700014, India. Tel: 244-5767/244-8065.
- **XIV Annual Conference of Indian Rheumatism Association India**, IRACON-98, is being organised at Hyderabad from December 10 to 12, 1998. Contact: Dr G. Narsimulu, Organising Secretary, Nizam's Institute of Medical Sciences. Punjagutta, Hyderabad - 500 082, Andhra Pradesh, South India. Tel: (O) 0091-40-332 0332, Ext. 132, (R) 339 0916; Fax: 0091 - 40331 0076.

All India Scientific Conference on Pulmonary Medicine and Respiratory Critical Care 'Chest India 1998' is being organised at Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh in collboration with Internation Academy of American College of Chest Physicians, from December 11-13, 1998. Contact: Dr SK Jindal, Addl. Professor & Head, Department of Pulmonary Medicine, PCIMER, Chandigarh - 160012. Tel: (O) 541031-39, Ext. 391, (R) 712030. Fax: 91-0172-540401, 543078.

First July 1998: Indian Medical Association (IMA) is organising a **Doctor's Day** on Ist July 1998 in collaboration with SKIMS. Soura, Srinagar. For details Dr. Mir Nazir (Secretary), Department of Surgery, Room No. 35 SMHS Hospital.

Indian Dental Association (JK Chapter) is organising a Dental Conference in Sher-i-Kashmir International Convention Complex during the last week of **September, 1998.** For details contact: President Dr. Bashir Ahmad, Govt. Dental College. Srinagar, Kashmir Phone: 45415, 471557 Fax: 0194-455022 (Office)

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Letter from Chief Editor

It is indeed a great pleasure to present before our readers the 17th issue of JK~Practitioner. With this issue we are completing five years of uninterrupted publishing. The objectives of the journal remain same as outlined in the first issue of October 1994 — to provide a source of concise and authoritative material for continuous medical education for Students, General Practitioners, Specialists and Teachers. What is keeping us moving and in fact improving, is the constant valuable encouragement, suggestions and criticism from our well wishers. Last year the annual meeting, to celebrate the 4th year of the journal was attended by eminent doctors from here and abroad, who are actively involved with the journal as consultant editors, or are on the advisory and editorial board.

Their suggestions were noted and implemented immediately in the issues of 5th volume. However, there may be some more deficiencies, which should be brought in our notice so that it becomes more and more interesting and useful for our readers with the passage of time. I am now becoming more and more aware about our short comings, as well as the need in future issues to bring new topics, changes in format, and addition of more items related to medical sciences. This journal has already entered its name in International indexing, and very soon with the help of eminent doctors here and abroad it will be available on internet also. I am greatly thankful to all my colleagues who are continuously patronising and guiding me every day and every minute. I am happy that students, clinicians and Medical teachers are now eagerly waiting for new issues of the journal. if this trend continues and our finances permit we may add supplementary updates on various subspecialities along with the regular issues. I am greatly thankful to faculty of Nassa county (USA), especially Chairman Department of Medicine Prof. Farooq A. Khan (Regent American College of Physicians) Dr. Mir A. Afzal (Wales University UK) Dr. G.J. Mufti (Head Department of Haemato-Oncology, King's College U.K) and other colleagues abroad for reviewing our articles before acceptance. My thanks to Faculty of G.M.C. Srinagar/Jammu/SKIMS/PGI Chandigarh/AIIMS New Delhi/Safdar Jung Hospital/Jawahar Lal memorial Hospital (Aligarh)/Banaras Hindu Hospital (especially GIT Department)/Gangaram Hospital/G.B.Panth Hospital/ Apollo Hospital/Batra Hospital for contributing and for acting as our reviewers. Recently I had short meetings with some eminent scientists, doctors during their visit to Kashmir, Prof. Muzaffar Ahmad (Chairman Deptt. of Medicine Celevland, USA), Dr. Mir A. Rouf (Nephrologist, Kansas USA), Dr. M. Altaf Orthopaedician UK, Dr. Peerzada Farooq Cardiologist Boston, USA, Prof. M.S. Khuroo (Head KFSH, Riyadh KSA), Dr. G.H. Malik (Nephrologist, Riyadh), Dr. G.R. Mufti (Urologist UK), Prof. S.R. Niak (Sanjay Gandhi Institute of P.G. Medical Sciences, Luknow) & Prof. R. Bajaj (Dean, Sanjay Gandhi Institute of P.G. Medical Sciences Luknow) & Dr. Muzaffer Ahmad, Director Health Services (Kashmir).

JK~Practitioner is becoming a good if not a complete source of scientific data on various diseases prevelant in the State and is an inspiration for CME programmes for distant Institutes and Hospitals of the State. We at the same time are widening our base. Already a number of prestegious institutes of the country are becoming regular contributors. I am thankful to my Assistant/deputy editors who are putting all their effort to make the journal of International class especially my Deputy editors Dr. Zaffar A. Khatib and Fayaz A. Bhat Associate editor, Dr. R.K. Chrangoo and the advertising Executive Dr. M.L. Bhat. My thanks are due to Dr. Riaz Bashir and Dr. Showkat Bashir who are holding the fort in the USA.

G M Malik
MD, FACG
Chief Editor/Senior Consultant
Head GIT Division, Deptt. of Medicine,
SMHS & Associated Hospitals, Srinagar

Aggressive Management Strategies for Cardiogenic Shock Following Acute Myocardial Infarction

Cardiogenic shock remains a highly lethal event and patients with this condition complicating acute myocardial infarction are amongst the highest risk patients with cardiovascular disease. The incidence of this complication seems to have remained relatively unchanged over the years and varies from 5-15% despite the widespread use of thrombolytic therapy.[1,2] In GUSTO-1 trial cardiogenic shock was identified in 7.2% patients of the total of 41021 patients included. These patients had a 30 days mortality of 55% and accounted for 58% of all deaths in the entire cohort.[3,4] This strikingly high mortality is the result of several factors, including the size of infarction, recurrent infarction, ongoing ischemia and extension of infarction.[1] To optimize the treatment of these patients remains a challenge in cardiovascular medicine. Evaluation of the effect of various treatment strategies has also been difficult. An important limitation has been the selection bias. Patients felt to be 'hopeless' may not even be approached to enter randomized trials and significant number of patients entering a trial may succumb before a treatment plan can be carried out.

Data from several non-randomized and observational studies clearly indicate that the outcome of cardiogenic shock can be improved with measures to raise intra coronary perfusion pressure and supporting the systemic circulation (using intra aortic ballon counterpulsation and pharmacological agents) in association with restoring persistent brisk flow to the infarct territory (coronary angioplasty or coronary bypass graft surgery). The mortality rates as low as 30-40% have been reported in the literature using these strategies.[5,8] In this situation widespread use of intra-coronary stents seems to be of particular importance because of their property of very low acute and subacute closure rates.[9,10] Maintenance of TIMI-3 flow is of crucial importance in these very sick patients. Use of adjunct therapy like glycoprotein IIb/IIIa inhibitors also needs a careful evaluation.

In the GUSTO-1 study the 30 days mortality among shock patients treated in the United States was significantly lower at 50% vs 66% in the non US countries, a reduction of 24% (P<0.001).[11] This difference could be correlated to the pattern of care and resource utilization in US vs non US countries. Every invasive intervention was performed significantly more frequently in the US patients. This included cardiac catheterisation (58% vs 23%), intra-aortic ballon pump use (35% vs 7%), ventilatory support (54% vs 38%) and revascularisation by coronary artery bypass surgery (16% vs 9%) or coronary angioplasty (26% vs 8%).[12,13] This more aggressive invasive approach translated to a lower mortality rate even after adjustment for the baseline characteristics of patients in GUSTO-1 trial. Further analysis of the data showed that irrespective of the country, one year mortality was significantly lower in patients who underwent a PTCA with successful reperfusion.

It is a fact that at present there is no data from randomized trials substantiating the superiority of aggressive invasive reperfusion therapy in the management of cardiogenic shock. However there is compelling evidence that aggressive interventional measures aimed at providing reperfusion of the infarct related artery at an early stage in the natural history of cardiogenic shock can significantly improve the outcome of these very sick patients.[5,8] Two trials are currently underway to look into the role of angioplasty for the management of cardiogenic shock. Selection bias can however influence the results of these trials. This has been pointed out by Hochman et al[14] who found that selection for angiography in itself was associated with improved outcome irrespective of the nature of treatment administered.

The need of the hour is not to question the superiority of invasive treatment strategies but to identify those patients of acute myocardial infarction who are at high risk to develop cardiogenic shock. These patients should be offered aggressive invasive revascularisation therapy in order to maximise the benefit with optimal resource utilization.

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JK- Practitioner 1998;5(4): *248-249*

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VATS-Video Assisted Thoracic Surgery (A new horizon in non invasive Surgery)

Older therapeutic interventions are occasionally resurrected, refitted with current technological hardware or reapplied to novel problems under the guise of "new techniques." Thoracoscopy whose use was actually described over 88 years ago[1] is a good example. With the development of miniature cameras and the ability to display the image into the video screen, major changes occurred first in General Surgery with Laparoscopic Cholecystectomy taking the lead and establishing itself in an era of minimally invasive surgery. Although thoracoscopy was primarily developed as a diagnostic procedure in 1910 it was soon used for "adhesiolysis" in the treatment of or tuberculosis.[2] However real dramatic advances came when world was witnessing an era of minimally invasive surgical techniques which had made significant impact in lowering morbidity and mortality and in changing the indications for operative surgery. The standard open thoracotomy infamous for its post operative pain and attendant complications, is already being replaced in a large number of siutations by minimal invasive video assisted thoracoscopic techniques. Thoracoscopy has provided the thoracic surgeons with a safe and powerful tool, to have access directly into the chest for diagnosis of inaccesible lesions by conventional diagnostic procedures such as bronchoscopy and trans thoracic needle aspiration and simultaneously can be treated without open thoracotomy.[3] The main advantage of thoracoscopic surgery is the reduction in post operative pain and disability following an operative procedure. Early return to work, has reduced the disability costs. While evaluating this technique, the reduction in pain and disability must always be balanced against the ability to perform the procedure well and any increased risks that may be incurred. Any operation done through the thoracoscope must be able to the performed at least as well as what can be done via thoracoscope. There are amny prerequisites for such type of surgery agreed by Joint Committee on Thoracoscopy and VATS (video assisted throacic surgery) of American association including the following.; (a) Surgeon who has an experience in Thoracic surgery and can deal with the complication when arised. (b) VAT surgery makes a special demand on the Anesthetist. The separate ventilation of both lung lobes, good knowledge in thoracic anesthesia is essential pre requisites for this type of Surgery. (c) The infrastructure of the hospital must be complete for successful throcoscopic surgery. (d) Appropriate equipment's and instruments.[4] There are many advantages for VAT surgery, instead of painful thoractomy incision with separation of ribs, two or three approximately 1.5 cm long incisions are required which results in less post operative pain and earlier mobilization.[5] There will be better view of the operative field due to magnification and enlargement of the field. In the majority of the operations there is marked reduction in operation time, at least patient is saved from an uncosmetic scar with early return to home and work thereby reducing the hospital cost and bed occupation Indication of VATS procedures are many, including the resection of the bullae of the lung, parietal partial pleurectomy for recurrent or persisting penumothorax, closure of parenchymal leaks, pleurodesis for recurrent pleural effusion, empyema, evacuation of haematoma, lung biopsies, biopsy of mediastinal lymphatic nodes and tumor, pericardial fenestration, thoracic sympathectomy, closure of thoracic duct leaks for chylothorax, esophagocardiomyotomy in selected patients,[6] and many more are added to the list like its use in interstitial disease of lung[7] resection of benign[8] and malignant tumors of the esophagus[9] thereby showing the expanded applications of diagnostic and therapeutic thoracoscopy.[10] So VAT surgery is gaining world wide acceptance in modern surgical concepts, which is due to its minimal invasiveness. minor trauma and less post operative pain, short hospitalization, earlier fitness for work and lower cost in over all compared to open surgical intervention[11]. The true role of VATS in the management of chest disease has to be examined in the context of local socio-economic factors. To qualify as a real advance in medicine, a new surgical approach has to be cost-effective.[12] However its low cost in developing world needs further probe and evaulation, as the role of Laparoscopy has recently been challenged in that part of the world[13] VAT has a promising future, by using it wisely, in carefully selected patients. Inspite of its wide spread optimism and criticism, as every new technique faces, it should be possible to combine with aspirations of minimal morbidity with previously documented excellent results of standard surgical practice. Despite its limitations especially in its cost and availability of optimal set up VATS should be within the armamentarium of every thoracic surgeon today. It is recommended that before any traditional thoracotomist switches to the VATS surgery, should have an experience and join some training program to get credentials from any Thoracoscopic society[14] and evaluate his own set up to be ready for VATS surgery. It is estimated that thoracoscopic procedures will make 20-30% of all thoracic interventions in the future.

We started this kind of treatment in King Fahad Hospital Medina-Munawarah four years back, after getting credentials from the Thoracoscopic society of United Kingdom, and are continuing with this modality in diversified thoracic problems as indicated above, with encouraging success and simultaneously improving our skills and technique, and operating time, without compromising patient safety standards.

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Gastric Cancer-Today's Facts and beyond

Gastric cancer ranks 14th in incidence among the major cancer types in US, however, it accounts for 7% of all cancers in males and 3% in females in India[1]. Japan, Eastern Europe, Sourth America (Chile, Costa-Rica) and in certain parts of Asia it seems to have epidemic incidence. Time-trends of this malignancy reveal a decline in its incidence over the past 60 years, nevertheless, the number of the newly diagnosed patients having Adenocarcinoma of the proximal end of stomach and GE junction (Taken as one disease) has dramatically increased in the past 15 years. Socio-economic reasons, N-nitroso compounds, smoking, gastric surgery, exposure to radiation, pernicious anemia, Blood group 'A' are old etiopostulates and H. pylori, family history, consumption of fruits and vegetables (inverse relation) are the neo-stresed risk factors. An interesting and locally relevant fact is the positive correlation between salt intake (sodium chloride) and the stomach cancer-the salt hypothesis, supported internationally[2,3,4,5,6,7]

Epidermal growth factor receptor (EGFR) overexpression occurs in 29.6-46.6% of gastric cancers and co-expression of Transforming growth factor alpha (TGF) correlate with the disease progression and poor prognosis. More than 5-fold amplification of erb-B2 (Her2/neu) protooncogene, homologous to EGFR is reported in the intestinal type of gastric cancer. Similarly C-met and K-sam protooncogenes are associated with schirrous type of gastric cancer[8].

The staging of the Gastric cancer is limited by inability of the imaging techniques (like CT/MRI) to detect tumor deposits in the normal sized lymph nodes and liver-mets. Endoscopic ultrasonography is promising at the moment for regional staging of the gastric cancer by precise imaging of the tumor depth and the peri-gastric nodes. Of late, Laproscopy has evolved as an accurate staging modality in assesing the stage of the disease, identification and sampling of hepatic/regional nodel disease and detection of small volume peritoneal disease, unappreciated by other non-invasive staging modalities (like CT/MRI/EUS). CT seems superior in the detection of distant metastases and MRI is unproven in the detection of invasion of adjacent organs.

Everisince, Theodore-Billroth in 1881 in Vienna successfully performed the first gastrectomy for Gastric cancer, surgical treatment remains the only known effective curative therapy and a principal determinant of survival even today. Surgical decisions and a complete ressection (Ro-ressection of the gross and microscopic disease) is guided best by the initial determination of the stage. Microscopic MI in absence of obstruction/bleeding are not ressected and are treated with supportive care/chemotherapy. A locally advanced but ressectable disease (defined on ultrasound as T3/T4) seem to have low potential for cure even after a complete ressection and pressently recommended to enter a neo-adjuvant chemotherapy protocol. Sonography TI or T2 seem to have a reasonable potential for cure and should be aggressively treated. Endoscopic ressection combined with high frequency ultra-sound is the latest in the treatment of early gastric cancer. Improving the overall survival in the gastric cancer will undoboutedly follow advances in the development of systemic treatment but will be dependent on accurate and thorough staging besides a very high quality surgery continuing to play a dominant impact on future treatment.

The initiation of post-operative therapy varies widely, however, data from the animal models suggest that the risk of peritoneal implantation and intra-abdomenal tumor dissemination after a laparotomy are high, providing a theoretical rationale for the immediate post-operative treatment and a delay of 5-8 weeks after surgery may allow the metastases to grow to a point where eradication seems difficult or even impossible. Scientifically designed and executed trials seems judicious means of advancing the clinical science in gastric cancer patients. Present day, 'Translational cancer research' involving the molecular properties to deterimen the natural history/response to therapy is quite popular. Two potential molecular determinents for the response in the gastric cancer, namely, Thymidylate synthase (TS) the enzyme targeted by Fluorouracil (5FU) and the excision-repair-cross complementing gene family-I (ERCC-I), a gene influencing the tumor's ability to repair intra-strand cross linking of cisplatin induced damage and has pivotal role in cell-cisplatin resistance, are inversely related to the response, survival and the ultimate prognosis. PCR quantitation of the intra-tumoral TS-mRNA level by tumors ascessible by endoscopic/core needle biopsies and the reverse-transcriptase PCR is used to analyse mRNA levels of ERCC-I. In a recently conducted study in 65 newly diagnosed gastric cancer patients, having a median follow-up of 27 months, the median survival for the entire cohort was 10 months, however, analysis of survival by stratifying the patients according to the median TSmRNA levels, 32 patients whose pre-treatment levels were $<4.6x10^{-3}$ have a median survival of 43+ months compared with a median survival of 6 months with pre-treatment levels of $4.6x10^{-3}$ (p=.004). Similarly another study having a median follow-up period of 3.9 years for 38 patients analysed for ERCC-I mRNA levels, the median survival is 10.4 months. The median survival for the patients with primary gastric cancer having ERCC-I mRNA level of $<5.8x10^{-3}$ (median) is 24 months compared to 5.4 months in patients with levels $>5.8x10^{-3}$(P=.034).[9]

Post-operative adjuvant strategies lack decisive benefit in improving the overall survival nevertheless, these are designed to treat gastric cancers who appear to have ressectable (curable) tumors and remain attractive because they offer systemic chemotherapy to a greater number of patients with a poorer prognosis than post-operative programme. There is no chemotherapy combination emerging as standard in the gastric cancer as is of today, but the activity and the safety in adminstering 5 fluorouracil and calcium-leucovorin remains consistant. My observation in treating gastric cancer with this adjuvant therapy seems sptimistic not only in dealing with a biologically less aggressive tumor in the valley but also claiming improvement in performance-status, quality of life and objective improvement in majority of my patient population with gastric cancer.

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Medical Education: A Need for change

Improved health is now widely perceived as a factor in social advancement. Investment in health is increasingly seen as an investment in making individuals and society at large more productive. Health is also seen as a right and as an important facet of human development. Society wants to respond to people's health needs with health interventions that are relevant, efficient, affordable, and equitably accessible to all its members. Worldwide reforms in health sytems are under way with a view to achieving these goals.

Prospects of change

The future role and responsibility of the academic medical institutions should reflect the likely essential features of the future health system and the aptitudes that the medical practitioners will have to possess. Medical universities and colleges should be encouraged not only to shape their educational programmes accordingly, but also to devote energy and resources to the considerable task of creating opportunities for this new doctor.

Accountability

To be seen as forces of social progress, academic medical institutions must accept some degree of accountability to ensure that people's health needs are bettermet. To that end they should reexamine their mandate and the scope of their action to enable them to help make decisions relative to health care organisation.

With social and political pressures for cost-containment and cost-effectiveness, the education and research programmes and service involvement of academic medical institutions will receive increasing scrutiny. Medical colleges will need to determine to what part of society's health agenda they can best contribute, either by themselves or in partnership with others. Establishing links and creating new alliances with other institutions in the health sector and else-where will become essential.

Academic Autonomy

Although it is desirable for academic institutions to continue enjoying the autonomy that will let them fully express their creativity, they should devote much of their intellectual potential to addressing issues widely recognised by society as being of predominant importance. Academic autonomy is likely to be better preserved if the institutions themselves take the initiative in addressing these issues, thus averting the threat of external control.

Preparing for change

The future role and responsibility of the academic institutions should be delineated according to the probable essential features of the future health system and the essential aptitudes that health professionals, will have to possess in the new health care delivery environment.

Growing concern for quality in health care, efficiency, greater comprehensiveness and continuity of care are likely to emerge as main issues in future. Participation of individuals and communities in health affairs will become common. Greater emphasis will be given to population perspective in health. Policy makers and care providers will apply epidemiological reasoning widely, enabling them to understand the range of influences on health from other socioeconomic sectors and to identify more accurately risk factors and segments of the population in greatest need. The protection of the environment will be integrated into health programmes. Prevention programmes will increasingly be regarded as valid alternatives or complements to curative programmes; the integration of public health and clinical programmes will be regarded as crucial to reduce cost and increase efficiency.

The Doctor of the Future

The profile of the ideal health professional is that he should be a caregiver, communicator, decision maker, community leader and a good manager. To ensure durable impact of educational reforms, academic institutions must accept accountability for preparing future doctors to function properly in society. To be more responsive, academic institutions need active participation in improving the quality and coverage of health care services, guaranteeing the relevance of education and research to priority health needs, a constant endeavour to apply and disseminate efficient learning processes in health sciences, and firm involvement in quality assurance and assessment of technology.

Quality in Medical Education

Medical education plays a significant role in shaping doctors of present and future. Academic institutions set ideals and standards in many ways, and they must strive to maintain educational standards of unimpeachable quality. Quality in medical education should be seen in the context of relevance and efficiency of the educational programme, and optima fitness of the future doctor in the society. The aims of an academic institution include teaching, research, medical service, continuing education and social advocacy. In the pursuit of quality, these elements must be arranged as an integrated whole with appropriate balance. Each function should complement the other, leading to a synergistic outcome.

The quality of the educational programme depends on the quality of students, the curriculum, the learning experience, and the means of the student assessment. These in turn depend on the available facilities, the quality of teaching staff, and the system of management.

Examinations should assess not only knowledge and its application but also desirable competencies and attributes. In clincial examination, different decision-making approaches must be developed to suit different situations. Student assessment should reflect these differences in competencies.

For medical education, methodological improvement in quality determination is urgently needed. Assessment of students should combine both formative and summative components, and it should be criterion-rather than norm-referenced. The total quality approach can be used in medical education.

New Methodologies

Medical education must become more student-and learning-oriented, must place more emphasis on primary care, and must use new settings for education. Several new methodologies are receiving increasing emphasis in academic institutions. Educational researchers believe that the Problem Based Learning approach is especially effective in integrating principles from the basic sciences with specific clinical experiences. Another educational innovation is the use of standardised patients, both real and simulated, to provide standardised clinical learning experiences, and to reduce subjectivity in the assessment of the student's clinical performance. Academic institutions are also finding new ways to use computers to improve the effeciency of information storage and retreival, to assist in medical decision-making, and to provide educational opportunities. Computers are routinely used for electronic searches of the medical literature.

Establishing Standards

There is a need to define and assess the intellectual and educational dimensions of quality of medical education in the generic qualities. Equally important are dimensions of context and relevance. The context should reflect the pattern of morbidity in the country, the pattern of the health service and its quality, and cultural norms. The academic quality relates to academic infrarstructure, the academic tradition, the quality of students, the curriculum, the number of students, the standard of assessment, and postgraduate experience.

Standardisation of medical education though a difficult challenge is essential. The best way to ensure quality is by continuous improvement.

Looking Ahead

For medical education to be relevant and meaningful, the physical, socioeconomic, and cultural environment must be considered. Curriculum must change the most. A change in curriculum is one of the most fundamental ways of giving practical expression to the training of doctors in line with the new concept of health for all through primary health care. To improve quality and to achieve excellence in medical education, there is a need for change.

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Rhabdomyolysis and Acute Renal Failure

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Acute renal failure (ARF) associated with traumatic rhabdomyolysis in war injuries was first reported by Frankenthal in 1916[1]. Minawi in 1923 described further cases of crush injuries of muscle and postulated that the muscle damage somehow contributed to the renal failure[2]. However, the credit for present understanding of ARF following crush injuries is due to Bywaters and Beall who in the 1941 World War 2nd victims of bombing raids of London described in detail the pathophysiological mechanisms of rhabdomyolysis and ARF in this condition[3].

Structure and function of skeletal muscle in relationship to rhabdomyolysis:

There are approximately 600 skeletal muscles in the human body comprising 40 to 50 percent of the weight. Each muscle is composed of numerous muscle fibers 10 to 80 micrometer in diameter. In general, the fibers extend the entire length of the muscles. The muscle fiber is surrounded by the true cell membrane called sarcolemma. Surrounding individual muscle fibers is connective tissue called the endomysium which contains small blood vessels and nerves. Groups of muscle fibers are surrounded by Collagenous tissue into fascicles and the muscle is attached to the bone by the tendon formed by connective tissue at the end of the muscle[4-6].

Each muscle fiber contains innumerable myofibrils containing myosin and actin filaments which are large polymerized protein molecules responsible for contraction. The sarcolemma surrounds the cell matrix called sarcoplasm composed of the usual intracellular constituents like potassium, magnesium, phosphate, protein, enzymes and myoglobin. There is abundance of mitochondria which synthesize ATP needed for both muscle contraction and relaxation. ATP provides energy for the active transport of calcium into the sarcoplasm. Though metabolically similar, muscle fibers are of two types: slow and fast. Slow fibers have greater number of mitochondria of oxidative metabolism with abundant myoglobin (red fibers) and are utilized for prolonged sustained contractions. Fast fibers are predominantly glycolytic, have fewer number of mitochondria and scanty myglobin content (white fibers) and are used in sudden forceful contractions[4-6].

Eitopathogenesis of rhabdomyolysis:

Rhabdomyolysis is the process of release of muscle contents into the circulation (myoglobinemia) following injury to the skeletal muscle. Myoglobinuria follows myoglobinemia. Approximately 30% cases of rhabdomyolysis develop renal failure[7].

The causes of rhabdomyolysis are:

I. Traumatic
1) Crush syndrome
2) Physical Torture
3) Unaccustomed muscular activity

II. Non-traumatic
1) Vascular occulusion
2) Metabolic disorders
3) Muscle diseases
4) Toxins and Drugs
5) Prolonged Coma
6) Infections and envenomation
7) Heat stroke
8) Carbon monoxide Poisoning
9) Hypothyroidism

Traumatic rhabdomyolysis

The crush syndrome:

The crush injuries causing rhabdomyolysis, myoglobinuria and ARF were extensively studied in the victims of World War II. On postmortem examination, there was extensive skeletal muscle necrosis and specific pigment nephropathy in subjects buried under falling debris[3,8-10]. Such descriptions have also come from the victims of Beirut bombardment by the US Army in 1983[11] and more recently those of Armenian earthquake of 1988 in which 600 patients developed myoglobinuric ARF[12]. The intracellular concentration of water, sodium,

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choloride and calcium is increased by external pressure on the muscle and partly by impairment of activity of sodium potassium ATP. When the muscles are released from the crushing object there is further loss of water and electrolytes into the damaged muscle and myoglobin gains access to circulation during this time[13-15].

Physical Torture:

ARF following physical torture was first reported by our group from Kashmir (India) in 1993[16,17]. Beating of the skeletal muscles akin to crush injuries causes rhabdomyolysis and myoglobinuria. In these studies, emphasis has been put on considering the possibility of ARF rather than concentrating on superficial injuries in a physically tortured person. Further reports of ARF due to physical torture have come in 1995 from Israel wherein the condition has been described as pseudocrush syndrome[18] and from Pakistan[19]. In all these studies, the muscles were physically crushed during interrogation by the Police forces by blunt trauma using sticks, butts of guns, iron rods, leather belts, and electric shocks leading to rhabdomyolysis. Myoglobinuria and "forced dehydration" during torture were considered as pathogenetic mechanisms of ARF in these studies[17,18].

Unaccustomed Musclular Activity

Myoglobinuria and ARF may follow any condition involving violent and unaccustomed muscular activity[20-22]. The condition is characterizedby pain, swelling and tenderness due to skeletal muscle necrosis associated with myoglobinuria and renal failure[23]. Status epilepticus, status asthmaticus, prolonged labour during pregnancy and high voltage electric shock and tetanus have all resulted in ARF due to rhabdomyolysis[24-28].

Non-traumatic rhabdomyolysis

Vascular occlusion

ARF has been reported due to myoglobinemia and myoglobinuria following arterial emboli occuluding major blood vessels to the lower limbs and following cardiopulmonary bypass surgery[29,30]. Release of myoglobin into the systemic circulation following the restoration of blood flow to an ischemic muscle. Cases of ARF due to myoglobinuria have occured due to vascular occlusion in sickle cell disease[31].

Metabolic disorders

Hypokalemia as a cause of rhabdomyolysis has been described[32-35]. It has been suggested that arteriolar dilatation in the skeletal muscle occurs due to release of potassium from the contracting muscle into the interstitial fluid. This leads to increase in blood flow to muscle during exercise[36]. Knochel and Schlein demonstrated that electrically stimulated muscular exercise in potassium depleted dogs results in myonecrosis[32]. The authors concluded that potassium deficiency prevents the increase in muscle blood flow that would normally occur during exercise, resulting in rhabdomyolysis. Thus, a combination of exercise and hypoklaemia is detrimental to skeletal muscle metabolism.

Hypophosphatemia may lead to cellular injury due to severe depletion of ATP content of the muscle[37]. A decrease in intracellular inorganic phosphorus concentration may interfere with the regeneration of ATP from ADP and a level of 1.5 mg/dl (0.48 mmol/L) has been suggested as crucial minimum[23].

Muscle disease

Primary muscle disorders associated with rhabdomyolysis and ARF include glycogen storage diseases like Mc Ardle's disease (lack of phosphorylase), Tarui's disease (deficiency of phosphofructokinase), or the muscle lipid metabolic disorder due to absence of carnitine palmityl transferase. Abnormalities in glycogen or lipid metabolism result in a block of anerobic glycolysis that predisposes to the loss of integrity of the Sarcolemmal membrane and the liberation of myoglobin following exercise[38-40].

Polymyositis, dermatomyositis and tropical pyomyositis have been reported as causes of ARF following rhabdomyolysis[41-43]. Acute episodes of muscle necrosis can follow in muscle disease when subjected to the stress of exercise or intercurrent infection[44].

Toxins and Drugs

Alcohol is a common cause of rhabdomyolysis[55-58] due to different mechanisms. Stupor or coma due to alcohol is an important cause and myonecrosis occurs due to compression of the muscles by the own weight of the body[49]. The other factors are altered cell membrane metabolism due to alcoholic myopathy[50,51], and phosphate depletion which is a well known cause of rhabdomyolysis. Hypokalemia and hypomagnesemia common in alcoholics may potentiate alcoholic myopathy[32,2].

Myoglobinuria and ARF has been reported in heroin addicts due to multiple factors like coma and direct toxic effects of heroin or one of its contaminants[53-55]. Cocaine has been reported to cause myoglobinuria induced ARF due to abnormal postures and vasoconstriction causing ischemia of muscle and renal tubular injury[56,57].

Pentamidine[58], Paraphenylenediamine[59], Terbutaline overdose[60], high dose haloperidol[61], Doxepine and Nitrazepam[62] and Lovastatin[63] have been reported as cause of rhabdomyolysis and ARF.

Infections and Envenomation

Viral infections like influenza, echovirus 9 and Varicella zoster can cause myoglobinuria and ARF[64-66]. Direct invasion of muscle fibers has been suggested as one of the mechanisms of rhabdomyolysis. Some of the bacterial infections reported as causes of rhabdomyolysis and ARF are Legionnaire's disease, Salmonella and Brucella[67-69].

Myonecrosis, myoglobinuria and ARF is induced by envenomation by snake[70] and honeybee stings[71].

Prolonged Coma

Prolonged coma due to any cause leads to pressure myonecrosis. Due to prolonged pressure there is an interference with local blood supply causing loss of integrity of the muscle membrane and release of myoglobin[47,49].

Heat Stroke

Rhabdomyolysis and ARF has been reported in exertional as well as classical heat stroke. Heat stress causes rhabdomyolysis by interfering with glycolysis[72,73]. Potassium is necessary for maintaining cell membrane potential and hypokalemia interferes with glycogen synthesis[74,75]

Carbon monoxide poisoning

Carbon monoxide poisoning causes hypoxia by formation of monoxyhemoglobin and leads to rhabdomyolysis[70]. Hypothyroidism causes elevated creatine phosphokinase and sometimes frank rhabdomyolysis[70]

Mechanisms of myoglobinuric renal injury

Myoglobin has a molecular weight of 17800 and due to its small size is easily filterable by the glomerulus[76]. The intravenous injection of pure myoglobin does not cause ARF in normal animals but if made acidotic (ammonium choloride ingestion) and hypovolemic (water deprivation) ARF develops[10,11]. Infusion of saline and bicarbonate solutions early during rhabdomyolysis has prevented development of ARF favouring this postulation[77]. Heme protein toxicity of the renal tubules is due to three basic mechanisms: renal vasoconstriction, cast formation in the tubules and direct toxicity of tubular cells of heme proteins[78].

Renal hypoperfusion and vasoconstriction occur due to fluid thirdspacing in the damaged muscles[11] and by inhibition of the activity of the vasodilator nitric oxide by myoglobin[79]. Renal vasoconstriction can also be elicited by activation of the endotoxin cytokine cascade system by the damaged muscle[80].

Under acidic conditions myoglobin breaks down in the renal tubule to produce globin and ferrihemate, the latter being toxic to the tubular cells[70]. Myoglobin is freely filtered at the glomerulus and forms myoglobin casts in the nephron. The heme protein cast formation is determined by the heme protein concentration in the distal tubule and the urinary pH, aciduria favouring development of pigment induced ARF[44,81,82].

In addition to these vasomotor, nephrotoxic and obstructive elements pathogenic in myoglobin induced ARF, there are other toxic factors associated with rhabdomyolysis which seem to be operative in humans[83]. Hyperphosphatemia can potentiate ischemic and nephrotoxic renal damage[84]. Hyperuricemia contributes to intratubular obstruction[83]

Clinic Course and Diagnosis oof Myoglobin-induced ARF

The clinical course of pigment induced ARF in general is similar to other forms of ARF but has some distinctive features. In addition to myoglobin, skeletal muscle contains large quantities of creatine, uric acid precursors (Purines), Potassium, Phosphorus[84,85]. Following muscle injury, these substances are released into the general circulation. Significant hyperuricemia, hyperkalemia, hyperphosphatemia and hypocalcemia thus are distinctive features of myoglobin induced ARF[23]. Creatine phosphokinase (CK) is present in the skeletal muscle and raised levels of its MM isoform is specific indicator for rhabdomyolysis. Without ongoing muscle necrosis, the levels peak at 12-36 hours. The levels may rise to thousands or upto one million or more per liter of serum. Though levels of other muscle enzymes such as aldolase, lactic dehydrogenase or transminases are raised but in clinical practice their measurement dose not provide any additional useful information[70]. Myoglobin once released into serum is lightly bound to an-globulin and is quickly excreted in urine. A positive urine Stix test for blood in absence of red cells on microscopy indicates myoglobin or hemoglobin. From the clinical point of view dark urine and pink serum are indicative of hemolysis whereas dark urine and clear serum suggest rhabdomyolysis. Myoglobin has a plasma half life of 1 to 3 hours and disappears from plasma within 6 hours and the diagnosis of rhabdomyolysis may easily be missed if the muscle damage was transient and the patient did not develop renal failure[86]. Though specific radioimmunoassays and spectroscopic assays for both myoglobin and hemoglobin are available, a simple laboratory test may be used to distinguish the two pgiments[44]. To 5ml of urine, add 2.8 gram of Ammonium sulfate; allow the mixture to stand for 5 minutes and filter-Hemoglobinuria is indicated by a colored precipitate whereas colored supernatant indicates the presence of myoglobin. This test can be very useful in conditions where both hemoglobinuria and myoglobinuria are simultaneously present as in cases of physical torture[17].

The presence of pigment granular casts in urine is characteristic of rhabdomyolysis[87]. ARF due to rhabdomyolysis is associated with hypocalcemia in the oliguric phase and hypercalcemia in the recovery phase[88]. Once ARF is established, hypocalcemia is a consequence of hyperphosphatemia and partly due to reduced 1,25 dihydroxychole-calciferol levels.

The ratio of serum creatinine to urea is normally 1:10. Due to release of large quantities of creatine phosphate from damaged muscle and its conversion to creatinine, this ratio is raised. Hypoalbuminemia results from leakage of plasma components due to capillary damage[70]

Management

Better and Stein after their extensive studies on rhabdomyolysis concluded that hyperkalemia, hyperphosphatemia, hypocalcemia and metabolic acidosis occur early and even before azotemia. The authors suggest an early, aggressive volume replacement and forced alkaline-diuresis therapy to protect the kidney against ARF[13]. Isotonic saline solution is infused at a rate of 1.5 liters per hours as soon as a trapped person's limb has been freed. This is followed by infusion of hypotonic sodium chloride with 40 mmol of Sodium bicarbonate and 10 gram of mannitol as 20 per cent solution per liter. An adult may need upto 12 liters per day. This regimen will protect against the nephrotoxicity of myoglobin and urate and also control hyperkalemia and acidosis. Calcium infusion as treatment of hypocalcemia and hyperkalemia should be avoided unless the latter is causing life threatening arrhythmias[15].

The infused calcium besides correcting serum calcium only temporarily will get deposited in the traumatized muscle[89]. This will also increase the problem of hypercalcemia during the recovery phase of ARF.

Dialysis may be needed for severe metabolic disturbances like hyperkalemia in the oliguric phase or hypercalcemia in the diuretic phase[90]

In our study of 10 cases of ARF following physical torture, 9 neeeded dialysis[16].

Development of compartment syndromes may lead to persistent rhabdomyolysis and delay the recovery from ARF Fasciotomy may be needed to avoid tissue damage and avoid unnecessary amputations. Considering the infection of open wounds after fasciotomy Better and Stein have urged conservtive rather than surgical management[13]. Rainford and Stevens, however, recommend surgical exploration in all doubtful cases[68]. Myoglobin is pooly removed either by hemofiltration or peritoneal dialysis but even in presence of severe ARF the blood levels of myoglobin fall probably because of hepatic and splenic uptake[91].

Prognosis

Prognosis depends primarily on the underlying cause for rhabdomyolysis. The mortality from the crush syndrome is 60-70% usually due to sepsis and adult respiratory distress syndrome[44]. No mortality occurred in the ten cases of ARF following physical torture[16] whereas in another study 5 out of 34(15%) died, the cause being sepsis in 4 of them[17].

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Helicobacter Pylori Organism and its Prevalence in various Gastroinyestinal Disorders in Kashmir

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The presence of spiral organism in stomach was documented about a century ago but these were taken merely as contaminants and this ignored. A new thinking about these organisms called Campylobacter pyloridis began in 1981 when gastric mucosal bacteria were demonstrated by Barry Marshall and Robin Warren (Australians) after staining gastric biopsy speciment with Warthin-Starry stain. The first culture of Compylobacter pyloridis organism was reported on 22 October 1982[1]. These bacteria were renamed as Campylobacter pylori in 1987[2] but presence of multiple flagellae on these bacteria differntiated them from other Campylobacteria. Subsequently in 1989 new genus was suggested for these bacteria[3]. 'Helicobacter' reflects the two morphological appearences of the organism, helical in vivo and rod like in vitro.

Morphology

Helicobacter pylori is a Gram-negative, S-shaped or curved rod (0.5-0.9 um wide and 2-4um long), multiflageallate (with 4-6 polar flagella measuring 2.5 um in length and 30nm in thickness with a membraneous terminal bulb). H. Pylori also exists in coccoidal form especially on prolonged cultures.

Biochemical Characteristics

H. pylori produces catalase, cytochrome oxidase, urease, alkaline phosphatese, acid phosphatase, Leucine arylamidase, phospholipase A, mucinase, Lipase, Lipopolysaccharidase, Hemolysin, Leucotriene B4 and platelet activating factor which play important role in pathogenesis of various H. pylori related diseases like type B gastritis, peptic ulceration, gastric adenocarcinoma, MALT (mucosa associated Lymphoid tissue) lymphoma.

Genetic Characteristics

The size of H.pylori chromosome has been found to be 1.63-1.73Mb[4]. (determined by pulsed-Field gel electrophoresis-restriction Fragment length analysis) and at least 50 genes have been cloned from H. pylori. Several genetic determinants are implicated in the virulence of H. pylori e.g. vacuolating cytotoxin gene (VacA), cytoxin-associated gene (cag A), Flagellin gene (Fla A, Fla B), unrease gene cluster (Ure E, Ure F, Ure G, Ure H and Ure I required for Unrease activity) Pic A and Pic B (induces production of interleukin by gastric epithelial cells is a strong mediator of inflammation[5,6].

Transmission of Infection

The epidemiological studies show great variations in developed and developing countries like India, H. pylori infection is acquired earlier[7]. The factors affecting prevalence are related to socio-economic status and include hygiene, environmental contamination (water, food), income, level of education, housing density, overcrowding and locality of birth[8].

Man is the reservior of infection and actual route of transmission is unknown. Transmission may occur either by Fecal-oral or oral-oral route[9]. Higher prevalence of H. pylori infection have been found in endoscopists, staff of gastromterology sections, mentally retarded children, orphanages, mothers of H. pylori positive children and sexual partners of H. pylori positive persons[10].

Pathogenesis

H. pylori is a non-invasive organism found just below the mucus layer. It colonizes by producing urease and gastric acid inhibitory protein thereby escapes the on slaught of acidic pH. By virtue of polar flagellae approach mucus layer and mucinase produced by the bacteria disrupts and breaks down this barrier. It also adapts to the host environment by the help of heat-shock proteins. Direct damage to the host occurs by the production of urease and other enzyme besides via production of cytotoxins e.g Vaculolating cyotoxin-encoded by cytotoxin associated gene A(cag A) A DNA region called "pathogenicity island" is a marker of cytotoxicity and encodes proteins such as Pic A, Pic B which are involved in cytotoxic protein secretion, signal transduction and induction of cytokines such as IL-8[11-15]

Strain diversity explains why only 20% of individuals infected with H. pylori develope disease like peptic ulcer, gastric cancer, type B gastritis or MALT lymphoma. Host

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factors like immune responses, genetic factors besides environmental factors also influence the pathogenesis of H pylori infection.

H pylori infect antral D-cells (sources of somatostatin) and inflammation of these cells leads to their destruction. Through the liberation of various inflammatory mediators. Thus somatostatin levels get decreased and therefore gastrin levels are increased which lead to increased gastric acid output. The increased gastric acid gives rise to duodenal gastric metaplasia which gets infected with H. pylori leading to duodenal ulcer formation[16].

Diagnosis

Two types of tests are used to diagnose H. pylori infection-invasive and non-invasive. Amongst the invasive tests (where endoscopy is necessary) are rapid Urease test (RUT), Histology, Gram's Staining, culture and polymerase chain reaction. The non-invasive tests include serology and urea breath test (UBT).

Helicobacter pylori infection in various gastrointestinal disorders in Kashmir

1. Antral Gastritis

H.pylori infection has been strongly found to be associated with Type B (Chronic active gastritis) gastritis throughout the world in 90-100% of cases [17]. Our study also found a highly significant association between the two. H. pylori infection was present in 90% of peptic ulcer patients with associated antral gastritis whereas H. pylori was present in 87.50% of asympatomatic healthy volunteers with antral gastritis $(P<0.005)$[18].

Peptic Ulcer Disease

Kashmir valley is highly endemic area of peptic ulcer disease with a point prevalence of 4.72%[19]. The evidence which supports the role of H. pylori in the pathogenesis of peptic ulcer disease is that eradication of H. pylori leads to ulcer healing and reduces recurrences[20]. The association of H. pylori with duodenal ulcer was found to be 76.09% whereas the association with gastric ulcer was 50%[20]. There was no difference in H. pylori infection among males and females, smokers and non-smokers. Also our study did not find any relationship between ABJO blood groups and H. pylori psoitivity among Kashmir population[21]. The prevalence of H. pylori increased with advancing age but it was not of any statistical significance.

Gastric Cancer

Helicobacter pylori has been labelled as group I or definite Carcinogen in the pathogenesios of gastric cancer by WHO. It leads to acute gastritis which progresses to chronic atrophic gastritis, intestinal metaplasa, dysplasia and finally leads to intestinal form of gastric adenocarcinoma.

Kashmir has a very high incidence of gastric cancer[22] and H.pylori organism was observed in 34% of gastric cancer patients on histological examination (using Giemsa Stain)[23]. This implies that in Kashmir mere infection with H. pylori organism is not the only cause of such a high incidence of gastric cancer but there are other contributing factors as well. Also the isolation of H. pylori in less number of gastric cancer patients could be because of development of atrophic gastritis (as was noticed in a significant number of patients). There is at present no study to assess the association between H. pylori and MALT lymphoma in Kashmir.

Asymptomatic Healthy Volunteers

Compared to prevalence of 40-60% in various developed and developed countries, in Kashmir, H. pylori was isolated from 33.33% of asympatomatic healthy volunteers and H. pylori was present in 87.50% of asymptomatic healthy volunteers who had antral gastritis changes[18].

H. Pylori in NSAID Users

Since both H.pylori infection and non-steroidal anti inflammation drugs (NSAIDS) are important in the pathogenesis of peptic ulcer disease, a study was carried out to find the prevalence of H. pylori in relation to the occurance and severity of NSAID induced gastroduodenal injury[24]. This study did not find any significant difference in H. pylori infection among NSAID users and non-users (38% vs38.67%). However, among NSAID users, H. pylori infection increased with the severity of gastroduodenal lesions, thereby suggesting the H.pylori infection may potertiate the gastroduodenal toxicity of NSAIDS.

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- Myokymia
- Hemifacial spasm
- Tremor
- Tics
- Palatal myoclonus

C) Spasticity[13,14]

- Multiple sclerosis
- Cerebral Palsy
- Post Stroke
- Post Traumatic Myelopathy

D) Muscle Contraction Headache

E) Parasomnia

- Bruxism

II. Ophthalmological[4]

- Strabismus
- Acute Oculomotor Palsy
- Nystagmus
- Myokymia
- Protective Ptosis

III. Dermatological[15,16]

- Glabellar Wrinkless
- Crow's feet
- Nasolabial folds
- Horizontal forehead lines
- Hyperkinetic facial lines

IV. Miscellaneous[17-19]

- Masseteric hypertrophy
- Oesophageal achlasia
- Anal fissure
- Detrusor sphincter dyssynergia
- Anismus

Meig's syndrome is a relatively refractory dystonia with poor response to oral medication. There is no surgical treatment available for this entity. However, Botulinum toxin therapy has been found to be effective in over 70% of patients with oromandibular dystonia. In jaw closure and jaw opening dystonias, masseter and submental muscles respectively are injected with the toxin. Response has been found to be better with jaw closure dystonias. Transient swallowing problem has been observed in 1/3rd of the cases.[5]

Spasmodic dysphonia like oromandibular dystonia is also refractoray to anticholinergic and benzodiazepine drug therapy. Surgical therapy includes uni-lateral transection of the recurrent laryngeal nerve. However, BTX therapy is believed to be superior and more efficacious in this condition. After establishing the diagnosis of spasmodic dysphonia the toxin is injected through a monopolar teflon coated needle into the thyroarytenoid muscle under electromyographic (EMG) guidance. There are three methods of administration of BTX in spasmodic dysphonia which includes (a) unilateral EMG guided injection upto 30 units of the toxin into the thyroarytenoid muscle (b) bilateral injection of upto 4 units of the toxin into each vocal fold under EMG guidance (c) Injection of the toxin via indirect laryngoscopy without electromyographic assistance. The success rate following this therapy ranges from 70-95%. Untoward effects include hoarseness, transient hypophonia, dysphagia and aspiration. Abductor form of spasmodic dysphonia can be managed by injection of BTX into the posterior cricoarytenoid muscle.[6]

Botulinum toxin has been used in the treatment of voice tremor and stuttering with mixed results[12].

The treatment of carvical dystonias include pharmacotherapy, selective peripheral denervation and administration of BTX toxin. Pharmacotherapy is effective in about one dhalf of the cases. BTX therapy is effective in about 2/3rd of the cases and latency between the admdinistration of the toxin and onset of clinical improvement has been found to be about 1 week. The beneficial effect lasts for about 1 month. Untoward effects including dysphagia and focal weakness resolve within 2 weeks.[5,7,8]

Modalities of therapy for task specific dystonias include muscle relaxation techniques, occupational, medical and surgical therapies. By and large, all such modalities have yielded disappointing results. Botulinum toxin administration into electromyographically selected hand and forearm muscles have yielded encouraging results. Unwanted effects include temporary hand weakness.[9]

Botulinum toxin therapy in patients with striatal toe mitigates disability, pain and improves gait disturbances.[10]

Hemifacial spasm, a form of segmental myoclonus is treated with carbamazepine, phenytoin, baclofen and microvascular decompression (MVD) of the facial nerve.

Microvascular decompression is associated with irreversible facial weakness, deafness, stroke and occasionally death. Hence, local administration of BTX into selected facial muscles is a better mode of therapy. Amelioration of symptoms lasts for about 6 months. The predominant untoward effect includes facial paralysis.

Tremor, the most common movement disorder is associated with dystonia in about 50% of the patients. Apart from conventional drug therapy, BTX administration has been found to be effective in reducing the amplitude of tremor in about two-third of the patients. Transient local weakness following toxin administration varies from 10% to 60% in patients with head neck and

Botulinum Toxin - Clinical Applications

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Botulinum toxin is the most potent biologic toxin known to mankind. Its use has been made in a host of neurological, ophthalmological and dermatological conditions. The incidence of clinical botulism is less common as compared to iatrogenic botulism. Botulinum toxin is obtained from an anaerobic, gram positive, spore forming organism known as Clostridium botulinum. There are seven sero types of the toxin designated as Botulinum toxin A through G. These different toxins differ in their antigenic specificities. All the seven toxins are neurotoxins except for C_2. Active neurotoxin has a molecular weight of 150,000 daltons and comprises of a heavy and a light chain. The toxin is inactivated by boiling for 10 minutes whereas spores get inactivated at a temperature of 120°C.[1]

Mechanism of Action:

Botulinum toxin (BTX) acts by inhibiting acetylcholinc release at the neuromuscular junction. This involves binding of the toxin to specific receptors located on the presynaptic neuron of the neuromuscular junction followed by internalization of the toxin into the nerve cytosol by energy dependent, receptor mediated endocytosis. The final step consisting of inhibition of acetylcholine release is an enzymatic process that utilises zinc as a co-factor. The toxin exhibits poor penetration across the blood brain barrier and hence, does not produce CNS untoward effects. The chemical denervation brought about by botulinum toxin lasts for about 3-4 months.

Botulinum toxin being an immunogenic substance induces neutralising antibody formation.[2] These antibodies account for about one third of all treatment failures encountered in patients with various neurological disorders. The antibody formation is directly proportional to the amount of toxin administered. The problem of treatment failure consequent to antibody formation can be circumvented by switching over to another sero-type of the botulinum toxin because antibodies to one type generally do not cross-neutralise another sero-type of the toxin.

Botulinum toxin A (BTX-A) is harvested from a culture medium after fermentation of Clostridium botulinum. The toxin is diluted from milligram to nanogram concentrations, freeze dried and dispensed as a white powder. It has been seen that the heavy chain of BTX-B binds to the presynaptic neuron and the light chain prevents the release of acetylcholine by proteolytically cleaving synaptobrevin. BTX-D and BTX-F also cleave synaptobrevin at post synaptic membrane. However, BTX-A and BTX-E inhibit acetylcholine release by clearing SNAP-25 (Synaptosomal associated protein). BTX-C acts by clearing syntaxin which is embedded in the presynaptic membrane.[3] The distant effects of BTX injections have been attributed to retrograde transport of the toxin to the spinal cord neurons as well as the distribution of the toxin via the systemic circulation.

BTX diffuses upto 4.5 cm from the site of single injection as shown by animal studies. The area of paralysis is directly proportional to the dose and the cross-sectional area of the muscle injected. Multiple injections have been found to be more efficacious than a single bolus injection because multiple injections contain the biological activity at the requisite site. Moreover, frequency of dysphagia associated with BTX therapy can be reduced by half when multiple injections are performed. The unit for measuring BTX toxin potency is derived from a mouse assay. One unit of BTX toxin is the amount of toxin required to kill 50% (LD 50) of a group of mice. The potency of BTX manufactured by different laboratories is variable. One nanogram of UK toxin contains 40 mouse units wheras 1 nanogram of US toxin contains 2.5 mouse units.

Clinical applications:

I. Neurological Disorders:

BTX has been used in a host of extrapyramidal and hyperkinetic disorders with remarkable success.

A) Focal dystonias[4-10]

- Blepharospasm
- Meige's syndrome
- Cervical dystonia
- Writer's/musicians eramp (Task specific dystonias)
- Spasmodic dysphonia
- Striatal toe

B) Hyperkinesias[11-12]

- Benign essential blepharospasm

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hand tremor respectively.

The mainstay of treatment of tics includes dopaminergic antagonists. Occasional patients with disabling tics of neck musclutature have been treated with botulinum toxin injections with encouraging results. Unwanted effecdts include transient ptosis and nuchal pain.

Botulinum toxin has been used in various ophthalmological conditions as enumerated in Table II with variable results. Various dermatological/cosmetic conditions such as glabellar wrinkles, crow's feet, horizontal forehead lines and mesolabial folds have been treated with BTX therapy. Vertical glabellar frown lines result from over-activity of the corrugator superciliaris muscles with assistance from procerus and orbicularis oculi muscles. Contraction of these muscles is produced during negative emotions. The glabellar wrinkless can be made less conspicuous by administration of toxin into the corrugator supercilaris and orbicularis oculi muscles. Males require a slightly higher does than females for aforementioned cosmetic condition. The toxin should not be injected into the eyebrow as it will result in ptosis. The procedure is preferably performed with the use of Teflon coated electromyographic guided needles. Motor weakness is observed within 48 hours of injection and attains nadir by the end of first week. The efficacy of therapy is heralded by demonstration of "Botox Sign" which is characterized by wrinkling on both sides of the nose on attempting to frown. Complications of this mode of therapy include bruising at the side of injection, pain, headache and transient ptosis.[15,16]

Contraindications to BTX therapy; These are:-

a. Evidence of neuromuscular junction disorders like myasthenia gravis and Eaton-Lambert Syndrome.[20]
b. Motor Neuron Disease.
c. Concomitant administration of aminoglycoside antibiotics.
d. Pregnancy; Although BTX has been used in selected patients during pregnancy; however, its routine use has not been recommended in such a situation.
e. Patients wiht a known sensitivity to BTX or human albumin.

The introduction of botulinum toxin in the clinician's armamentarium has resolved many therapeutic aspects of a number of neurological and dermatological disorders. Moreover, with the availability of never serotypes of botulinum toxin in future, the menace of immunologically mediated treatment failures shall be overcome.

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Clinical Profile and Precision in Radiation Therapy in the Management of Gliomatous Tumours of Brain

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Abstract: *Radical surgical procedures of brain gliomas failed to improve results and secondly has limitation especially in lesions around brain stem. Another approach has been to combine surgery with conventional irradiation. This study explores the detailed clinical parameters and the precision in radiation therapy in patients having gliomatous brain tumours.Forty patients of clinically and histologically diagnosed gliomatous brain tumours were included in this study. All patients received treatment in the form of external beam radiation therapy. Gliomatous brain tumours are seen in two age peaks, one children and other in later life. Astrocytomas constituted (34/40) 85% tumours followed by medulloblastomas (4/40) -10%. There was significant improvement in signs and symptoms after radiation therapy. Fifteen (15/40) -37.5% patients had follow up of 6 months to 1 year till the conclusion of study and five patients (5/40) - 12.5% had a follow up of more than 1 year. Eighteen (18/40) 45% patients were capable of normal activity after radiation therapy. Seven (7/40) - 17.5% patients died during this study.*

Post-operative radiation therapy relieves the signs, symptoms and improves the survival quality in the patients with gliomatous brain tumours. To make therapy successful, patients need to attend at early stage, have investigations at right time. Further high precision, radiation therapy in the form of treatment planning system, conformal radiation therapy and radiosurgery are the need of time.

Key words: *Gliomatous brain tumour, External beam radiation*

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Introduction

Gliomatous brain tumours occur most commonly in all age groups and account for nearly less than 40% of all primary brain tumours.[1] These constitute 29-42% of primary brain tumours in India (reported by Ramamurthy) table I. The various gliomas are glioblastoma multiforme (20%), astrocytomas grade I and II (10%), ependymomas (6%), medulloblastomas (2%) oligodendrogliomas (1%) and papillma of choroid plexus (1%). Males are effected equally with females but astrocytomas are more common in males.[2]

Radical surgical procedures within the cranial cavity failed to improve results and secondly has its limitations especially in the lesions around brain stem. Another approach has been to combine surgery, conventional radiation therapy with chemotherapy, but randomised studies have failed to demonstrate any improvement.

Thus some form of combination treatment which in one modality in particular, the radiation therapy would need to modify its delivery is certainly the need of time.

The hazard of conventional radiotherapy is irradiation of normal brain tissue leading to brain damage. With conventional fractionation (180-200 rads/day given 5 fraction/wk) to a dose of 60 Gys, acute reactions are generally not fatal when they occur, usually manifested by evidence of raised intracranial tension or an exacerbation of symptoms or signs caused by lesion being treated. These reactions are due to oedema and usually respond to decongestive therapy.[3]

The present study is an attempt to evaluate:

1. Role of precision radiotherapy in the management of gliomatous brain tumour.
2. To study the clinical profile of the gliomatous brain tumours
3. To assess the role of radical radiotherapy in the management of gliomatous brain tumours with reference to subjective improvement, tolerance, regression in the size of tumour, adverse effects, disease free survival and overall results at the end of study.

Material and Methods

The study was conducted in the Department of

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Radiotherapy, Maulana Azad Medical College and associated Lok Nayak Jai Prakash Narain and Govind Ballah Pant Hospital, New Delhi. Also included are patients referred from other hospitals, nursing homes and other neighbouring states.

Forty patients with clinical and histopathological diagnosis of gliomatous brain tumour which included high and low grade Astrocytomas, Oligodendrogliomas, Ependymomas and Medulloblastomas were taken up for this study.

All these patients had a detailed general and systemic examination as detailed below:

1. Relevant history.
2. General physical examination and systemic examination.
3. Neurological examination.
   a) Higher cerebral functions
   b) Cranial nerves
   c) Motor system
   d) Reflexes
   e) Sensations
4. Investigations
   A. Routine Haematological, Biochemical and Radiological
      i) Haematological: Haemoglobin, Total leucocyte count, platelet count, peripheral blood smear and ESR
      ii) Biochemical: Liver function tests, Kidney fuctions tests
      iii) Radiological: Chest x-ray PA view, x-ray skull AP/Lateral
   B. Specific - C.T. Scan of Brain
      - E.E.G. (Electroencephalography)
      - M.R.I. scan of brain wherever possible

In all patients details of the surgical procedures were noted and emphasis given on site of lesion, nature of lesion, extent of the lesion and extent of surgical removal. All the patients were later subjected to treatment with radiation therapy.

Radiation therapy:

External beam radiation therapy was used to treat these patients. Megavoltage equipment- isocentric telecobalt therapy was used. Radiation therapy was delivered by different techniques individualised as per the location, nature and extent of the lesion. The following techniques were used:

1. Whole brain irradiation
2. Sectional brain irradiation
3. Multiple Beam Directed wedge technique.
4. Craniospinal irradiation.

The details of radiation techniques and time, dose, fractionation schedules used for different gliomatous brain tumours are depicted in table II and III respectively.

Isodose curves were drawn manually for all patient to optimize homogeneity of the radiation dose to tumour bed and to minimize the high dose region in the normal brain.

All the cases were clinically observed for raised intracranial tension, impairment or deterioration in neurological function and any other event during the course of treatment. Patients were followed up every 4 weekly and C.T. scan repeated at 6 weeks interval following completion of therapy then another at the end of study period.

Subjective and objective responses, tolerance ensuring complications, degree and duration of regression, disease free survival, quality of life and overall survival which are the main end points of the study were analysed and the conclusion drawn.

Results

Age & Sex: Majority of the patients belonged to age group of 30-39 and 50-59 years age group 20% each, followed by 40-49 years age group- 15%. Youngest patient was 5 years old and the oldest was 69 years of age. Male to female ratio was 3:1.

Tumour types: Table IV shows the distribution of the different gliomatous brain tumours taken in this study. Maximum number of patients were astrocytomas (34/40) -85%. 4 of 40 patients were medulloblastoma (10%) and none of this group had ependymoma.

Imaging techniques: X-ray skull done in all patients showed calcifation in two patients only. CT. scan was informative in all these patients. It delineated site of lesion in all patients and calcifation in 3/40 patients. MRI was done only in 3 patients because of technical reasons. Frontal lobe was the predominant site (10/40) -25% followed by parietal in 6 patients, temporal and frontoparital in 6 patients (6/40) -15% each.

Radiation reactions: Early radiation reactions (within week) were observed in 24(24/40) -60% patients in the form of headache, nausea and vomiting and rise in temperature. Early delayed reaction (weeks to month) were present in 6(6/40) -15% patients and late delayed reaction (months to years after completion of treatment) were seen only in 2(2/40) -5% patients.

Clinical assessment: Only five (5/40) -12.5% patients persisted with headache after radiation therapy treatment. Seizure showed marked improvement after radiation 2(2/40) -5% in comparison to 17(17/40) -42.5% before surgery. Similarly papilloedema and cranial nerve dysfunction reversed in the patients after surgery and after radiation therapy (Table V).

Karnofsky scale was used for assesing the performance of these patients. Only eleven (11/40) - 27.5% patients had performance status of 80-100% before surgery, fourteen (14/40) -25% after surgery and twenty (20/40) -50% after radiation therapy. This was statistically significant.

Follow up: Till the conclusion of this study, five patients (5/40) -12.5% had follow up of more than one year. Fifteen (15/40) -37.5% patients had follow up of 6 months to one year and twenty (20/40) -50% had follow up of less than 6 months.

Out of total, seven patients (7/40) who died, five of them belonged to grade III astrocytoma and two of them to grade IV astroglioma.

Quality of life: Eighteen (18/40) 45% patients were capable of normal activity. Limited capability was observed in only 5(5/40) -12.5% patients. Seven (7/40) -17.5% patients died after receiving radiation therapy, one died after nine months of completion of treatment and one patient died after 6 months of radiation therapy. Rest of the 5 patients died during first 6 months of irradiation. Residual tumour was presumed to be the cause of death in all these patients.

Medulloblastomas

Four (4/40) -19% patients had medulloblastoma in the age group of 9-30 years. Three (3/4) -75% were seen in the first decade of life. Male and female ratio was similar. Headache was the predominant symptom and cerebellar signs were present in three (3/4) -75% patients.

Surgical removal was attempted in all these patients. Craniospinal irradiation (35Gys/4 wks/5 fractions a week followed by 20 Gys/2wk/5 fraction a week to posterior fossa) was the radiation dose and technique used in these 4 patients. Three (3/4) -75% patients were followed upto 6 months and one followed upto more than one year. There was no mortality observed in this group of tumours.

Discussion

Brain tumours are known to occur in two age peaks, one in childhood, the other in later life (50-70 years of age).[4] In our study as well, there were 5 patients (5/40) - 12.5% of the paediatric age group. In contrast to Ramamurthy's[2] observation of equal incidence among males and females, the majority of the patient in our study were males (30/40)_ -75%. Male to female ratio was 3:1.

Astrocytomas constituted the main bulk (34/40) -85% in the present study followed by medulloblastomas (10%) and oligodendrogliomas (2.5%). Higher incidence of astrocytomas have also been described by Gehan, E.A. Walker[5] and Ramamurthy.[2]

Headache was the predominant symptoms followed by seizures in 42.5%, disturbance in motor symptoms in 35% and papilloedema was present in 50% of patients in our study. Penfield et al[6] found that about 2/3rd of slow growing astrocytomas and only 1/3rd of glioblastomas had fits at some stage. C T. scan was highly informative in all patients which revealed the site of lesion, calcification and oedema. Frontal lobe was the predominant site of lesion (25%) followed by perietal and temporal (15% each). These findings are consistent with other authors.[1,7]

With the advent of modern megavoltage equipment and the sophisticated technique using beam directed small field radiation therapy, it has been possible to deliver a desirable tumour dose to the target volume in order to achieve the desired effect without jeopardizing the normal tissue in the cranial cavity.

Routine postoperative irradiation of 50-60 Gys to limited radiation fields depending on accurate surgical and radiological assessment of tumour extent with adequate treatment margins is recommended. Daily tumour doses ranging from 150 to 200 rads with four or five fractions/week are to be delivered.[8]

Different authors have given different schedules but treatment fields must be generous and a dose beyond 40 to 45 Gys to whole brain especially for young patients with less aggressive tumours is not recommended.[8]

In contrast to our observation, James E. Morks[9] found pathologically documented cerebral radionecorosis within a median time of 14 months after completion of treatment in 7 of 139(5%) patients who received 45 Gys or more using 180-200 rads/fraction.

As shown in table V there was a marked improvement in clinical symptomatology after radiation therapy. Thomas R, Whyte et al[10] also observed a significant clinical improvement after radiation therapy in patients with brain stem gliomas.

Follow up and survival

Five patients (5/40) -12.5% had follow up of more than one year and 15 patients (15/40) -37.5% had follow up of 6 months to 1 year till the conclusion of this study.

Median survival of 18-40 wks has also been reported by Gehan EA, Walker[5] while studying the prognostic factors for patients with brain tumour.

Walker et al[11] observed approximate median survival time as 36 weeks in malignant gliomas while using whole brain radiotherapy. Similarly post-operative irradiation significantly prolonged life quality in astrocytomas of the brain as observed by Steven A. Leibal[3] similar to the conclusion drawn from our study.

Improvement in the quality of survival was also observed by John T. Fazekes[12] in the study of radiotherapy as treatment modality in Grade I & II astracytomas of brain.

Bloom et al[13] reported that 18/22 patients surviving five years or more had no serious disability and were leading normal life.

Outcome

In the present study 7 patients (7/40) -17.5% died during the course of this study. Five patients died during the first 6 months of treatment and the rest two died after 6 months of completion of treatment. Residual tumour was the cause of death in all the 7 patients.

Virtually no patient with grade IV tumour survives 5 years following treatment. Approximately 35-50% of treated patients with high grade astrocytoma, survive 1 year, but less than 20% survive 2 years. For grade III lesions 65-70% are seen to survive 1 year, 40% survive 2 year and 10-20% will survive 5 years or more.[8]

Death rate for patients with glioblastoma multiforme was 1.5 to 2 times higher than for those with malignant gliomas (48). This observation relates well with our results as well where high grade astrocytomas had a higher mortality rate.

Medulloblastomas

Considerable evidence has accumulated demonstrating the improved local control and overall survival following higher posterior fossa doses in excess of 50 Gy (48), similar to the dose used in the present study.

Hirsch J.F.[14] after conducting a study in 57 patients of medulloblastomas found that 5 years survival rate was 54% and rose to 71% patients who completed treatment with radiotherapy. These results can not be compared with our study having limited follow up.

By and large patients with intracranial tumours mostly present at a very late stage which poses problem to make any definite treatment modality successful. This is besides the nonavailability of sophisticated imaging tools at every centre. To make therapy more successful, patients need to attend at an early stage, have investigation at right time and very high precision equipments like treatment planning system, confermal radiation therapy and radiosurgery are the need of the time.

Table I: Incidence of intracranial tumors in different centres in India

Types of tumor	A Bombay	B Delhi	C Vellore	D Madras
Total	12015	1029%	1368%	1543%
Gliomas	35.22	42.54	35.8	29.3
Meningiomas	9.2	14.73	10.8	10.3
Schwanomas	6.9	8.09	9.2	9.9
Pituitary tumors	3.9	13.07	10.2	11.7
Developmental tumors and cysts	2.9	4.77	4.8	4.6
Granulomas	21.6	5.19	10.2	20.5
Secondaries	9.8	1.25	4.5	6.5
Miscellaneous	10.9	10.36	4.3	6.2
Gliomas when granulomas are excluded	50.0	44.9	53.0	36.0

A = Dastur and Lilitha (1976)
B = Tandon (1975)
C = Rath et al (1967)
D = Ramamurthi (1975)

Table II: External radiation therapy - techniques used Gliomatous brain tumours

Radiation technique used	No. of patients	Percentage
1. Whole brain irradiation	24	(24/40) 60.0
2. Whole brain irradiation followed by sectional brain irradiation	9	(9/40) 22.5
3. Whole brain followed by multiple beam directed wedge therapy	15	(15/40) 37.5
4. Craniospinal irradiation followed by posterior fossa boost	4	(4/40) 10.0
5. Multiple beam directed wedge therapy only	7	(7/40) 17.5
6. Sectional brain irradiation only	5	(5/40) 12.5

Table III: External radiation therapy - Time, dose and fractionation - Gliomatous brain tumor

Time, dose and fractionation	No. of patients	Percentage
1. 50 Gy/5 weeks/5 fractions a week to tumor bed (for low grade gliomatous tumors, low grade astrocytomas, oligodendromas and mixed gliomas)	10	(10/40) 25
2. 50 Gy/6 weeks/5 fractions a week whole brain followed by 15 Gy/2 weeks/5 fractions a week to residual tumor bed (High grade gliomas)	24	(24/40) 60

3. 35 Gy/4 weeks/5 fractions a week to craniospinal axis followed by 20 Gy/2 weeks/5 fractions a week to posterior fossa (for medulloblastoma	4	(4/40) 10
4. 50 Gy/6 weeks/5 fractions a week to tumor bed (for Brain stem glioma)	2	(2/40) 5
Total	40	100

Table IV: Types of gliomatous brain tumours

Tumor types	No . of patients	Percentage
Astrocytomas Grade I & II	8	(8/40) 20.0
Astrocytoma Grade III	18	(18/40) 47.5
Medulloblastomas	4	(4/40) 10.0
Astrocytoma Grade IV (Glioblastoma multiformis)	6	(6/40) 12.5
Endymomas	Nil	- -
Oligodendroglioma	1	(1/40) 2.5
Brain stem glioma	2	(2/40) 5.0
Mixed glimas	1	(1/40) 2.5

Table V: Clinical symptoms and signs before and after surgery and after radiation therapy 40 patients of gliomatous brain tumours

Clinical symptoms	Before surgery		After surgery		After radiation therapy	
	No. of patients	%age	No. of patients	%age	No. of patients	%age
Headache	32 (32/40)	80.0	25 (25/40)	62.5	5 (5/40)	12.5
Seizures	17 (17/40)	42.5	9 (9/40)	22.5	2 (2/40)	5.0
Motor symptoms	14 (14/40)	35.0	10 (10/40)	25.0	6 (6/40)	15.0
Personality changes	7 (7/40)	17.5	5 (5/40)	12.5	3 (3/40)	2.5
Speech alteration	3 (3/40)	7.5	2(2/40)	5.0	1 (1/40)	2.5
Nausea and vomiting	7 (7/40)	17.5	3 (3/40)	7.5	1 (1/40)	2.5
Sensory changes	-	-	-	-	-	-
Cranial nerve palsy	10 (10/40)	25.0	6 (6/40)	15.0	4 (4/40)	10.0
Cerebellar signs	3 (3/40)	7.5	2 (2/40)	5.0	1 (1/40)	2.5
Papilloedema	20 (20/40)	50.0	6(6/40)	15.0	2 (2/40)	5.0

p value > 0.5 p value < 0.05

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Pathology and Site Distribution of Gastric Adenocarcinoma in Kashmir

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Abstract: 738 resected specimens adenocarcinoma were studied over a 13 year period. The commonest histologic type was the intestinal type (65.58%) followed by the diffuse (27.10%) and colloid carcinomas (7.32%). The majority of cases of both intestinal and diffuse type were in the fifth decade (51.65% and 52%) respectively whereas the majority of cases (42.6%) of colloid carcinoma were in the sixth decade. Males were four times more affected than females. The commonest site was the antrum ana pylorus (42.30%) followed by the body (34.0%). Majority of both types of cancer were 2-5 cms in diameter. Ulcerative type was the commonest (62%) followed by the polypoid (24%) and diffuse types (14%).

Key words: Gastric carcinoma, Intestinal type, Diffuse type, Environmental cancer.

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Introduction

Gastric carcinoma is a very common cancer seen in this part of the country[1,2]. Its incidence in different Indian series varies from 3.4% to 25%[3-5]. This study was undertaken to study the pathology and site distribution of different types of gastric adenocarcinoma, to classify the carcinoma as per Lauren's classification[6] into the intestinal and diffuse types, to study the differences if any between these types and to see whether the morphology of gastric cancer differs in this part of the country as compared to the other states.

Material and Methods

738 resected specimens of gastric carcinoma were studied during a thirteen year period (January, 1983 to December, 1995). These specimens were opened and grossly examined in detail. They were fixed in 10% buffered formalin overnight. The tissues were then processed for routine paraffin embedding and 6-8 blocks taken from each specimen, 5u thick sections were cut and stained with the hematoxylin and eosin stain. All the slides were also stained by the PAS-Alcian blue technique PH 2.5 to demonstrate acid and neutral mucins, the former staining magenta and the latter blue.

Observations

The tumours were classified on histopathology according to the Lauren's classification into the intestinal and diffuse types, based on the predominant pattern of growth. Colloid carcinoma described by Lauren as arising from both the intestinal type and the diffuse carcinomas were studied as a separate group. Distinct, large, glandular lumina were typical of intestinal type carcinoma (Fig. I). They were often accompanied by papillary formations. In diffuse carcinomas cells were scattered either singly or in small clusters (Fig. 2). Glandular lumina were rarely seen and if present were small and indistinct. Colloid carcinomas arose from both intestinal and diffuse types but this formed the predominant pattern. These resembled the colloid carcinomas of the colon. Either dilated glandular lumina with rupture and profuse mucus secretions were seen or masses of mucus in which were embedded isolated cells or loose cell clusters.

The commonest histologic type was the intestinal type (65.58%) followed by the diffuse (27.10%) and colloid carcinoma (7.32%) (Table -I).

Age: The age ranged from 20-80 years. The majority of the patients were between 41 to 60 years of age (79.40%), 43.09% being between 41-50 years. 12.88% patients were below 40 years of age (Table-II).

The majority of both intestinal and diffuse types were between 41-50 years of age (51.65% and 52% respectively). However, the majority of cases of colloid carcinoma (59.30%) were above 50 years of age (Table-III). 10.74% patients with the intestinal type carcinoma were 40 years of age, or below, the peak incidence was in the 5th decade, 37.16% were above 50 years and only 4.55% above 60 years of age (Table-III). 12.5% patients of diffuse carcinoma were 40 years of age or below, the peak incidence was in the 5th decade, 35.5% were above 50 years and only 4.5% above 60 years of

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age (Table-III). In colloid carcinoma however, only 3.7% were below 40 years of age. 39.3% were less than 60 years old, the majority of the cases (42.60%) were in the 6th decade and 59.30% were above 50 years of age (Table-III).

Sex: Overall, males were affected four times more than females (4.2:1). The great majority (83.06%) of cases with intestinal type carcinoma were males (4.9:1). The male preponderance was less distinctly marked among patients with diffuse carcinoma (75% males, 25% females, 3:1).

Gross Pathology

1. Site: The commonest site was the antrum and pylorus (42.3%) followed by the body 29% & then G.E. Junction comprising 23% of the cases (Table IV). In the pylorus and antrum, the distribution was intestinal type 33.5% and diffuse type 37.2%. The gastroesophageal junction was involved in 26.86% of the intestinal type as compared to 16% of the diffuse and 14.82% of colloid types.

2. Size: Majority of the cancers were between 2-5 cms, in diameter (intestinal type 60% and diffuse type 59.9%). In contrast colloid carcinoma was larger being between 6-10 cms in diameter in the majority of cases (45.45%). Only 4.4% cases were less than 2 cm in diameter.

3. Type: The macroscopic features of the tumour showed some correlation with the histological main types. The ulcerative type was the commonest type (62%) in all the different types of carcinoma followed by the polypoid (24%) and diffuse types (14%). However, diffuse involvement of the stomach of the linitis plastica type was seen more in diffuse (19.1%) and colloid carcinomas (20%) as compared to the intestinal type (4.2%). The polypoid types was also seen more in the intestinal type (33.5%) than the diffuse type (16.8%).

Discussion:

Gastric carcinoma is among the commonest tumours in certain regions of the world e.g. Japan, Iceland and Finland. In the Kashmir valley, a very high prevalence rate has been reported[1,2] which is similar to the Western studies but much higher than that reported from other parts of India[3,7,8]. The present study reaffirms the high prevalence of gastric carcinoma in Kashmir. The majority of cases were between 41-50 years of age which is as decade earlier than other studies[4,7,8]. However, colloid carcinoma occured a decade later. Histologically two-thirds of the cases were intestinal type which has been described as the environmental type of gastric carcinoma. One third of the cases included diffuse and colloid carcinomas. This is similar to the observations of other workers[5,9]. However, Usha et al[7] have reported a higher incidence of the diffuse type. A number of authors[10-13] have studied gastric adenocarcinoma using Lauren's classification and it has been indicated that there are different etiological and eipdemiological factors for these two histological entities. The intestinal type is thought to be caused by environmental factors and predominates in areas of high incidence of the disease. This thus holds true for this place also. The diffuse type is thought to have a genetic predisposition with equal world-wide distribution. The ulcerative type was the commonest morphologic type found in our study.

This study thus shows (a) a high prevalence of the intestinal type of gastric carcinoma in this geographical region, (b) an early age of presentation of both the intestinal and diffuse types, (c) highest prevalence of colloid carcinoma in the sixth decade, (d) intestinal type was 4.9 times more common in males, (e) the commonest site was the pylorus and antrum followed by the body and the gastro-oesophageal junction, in the intesntinal type which also commonly presented as a polypoid tumours.

This study thus shows a different spectrum of gastric carcinoma here than the rest of India. The spectrum of gastric carcinoma in this region is thus quite similar to its counter part in the West.

Table-I: Showing the Histological types of gastric carcinoma

	Males		Females		Total	
Type	No.	%age	No.	%age	No.	%age
Intestinal	402	67.45	82	57.75	484	65.58
Diffuse	150	25.17	50	35.21	200	27.10
Colloid	44	7.38	10	7.04	54	7.32
Total	596	100.00	142	100.00	738	100.00

Table-II: Showing the age and sex distribution of gastric carcinoma

	Males		Females		Total	
Age (years)	No.	%age	No.	%age	No.	%age
11-20	1	0.17	-	-	1	0.14
21-30	10	1.68	2	1.40	12	1.63
31-40	54	9.07	28	19.72	82	11.11
41-50	254	42.61	64	45.07	318	43.09
51-60	225	37.75	43	30.28	268	36.31
> 60	52	8.72	5	3.53	57	7.72
Total	596	100.00	142	100.00	738	100.00

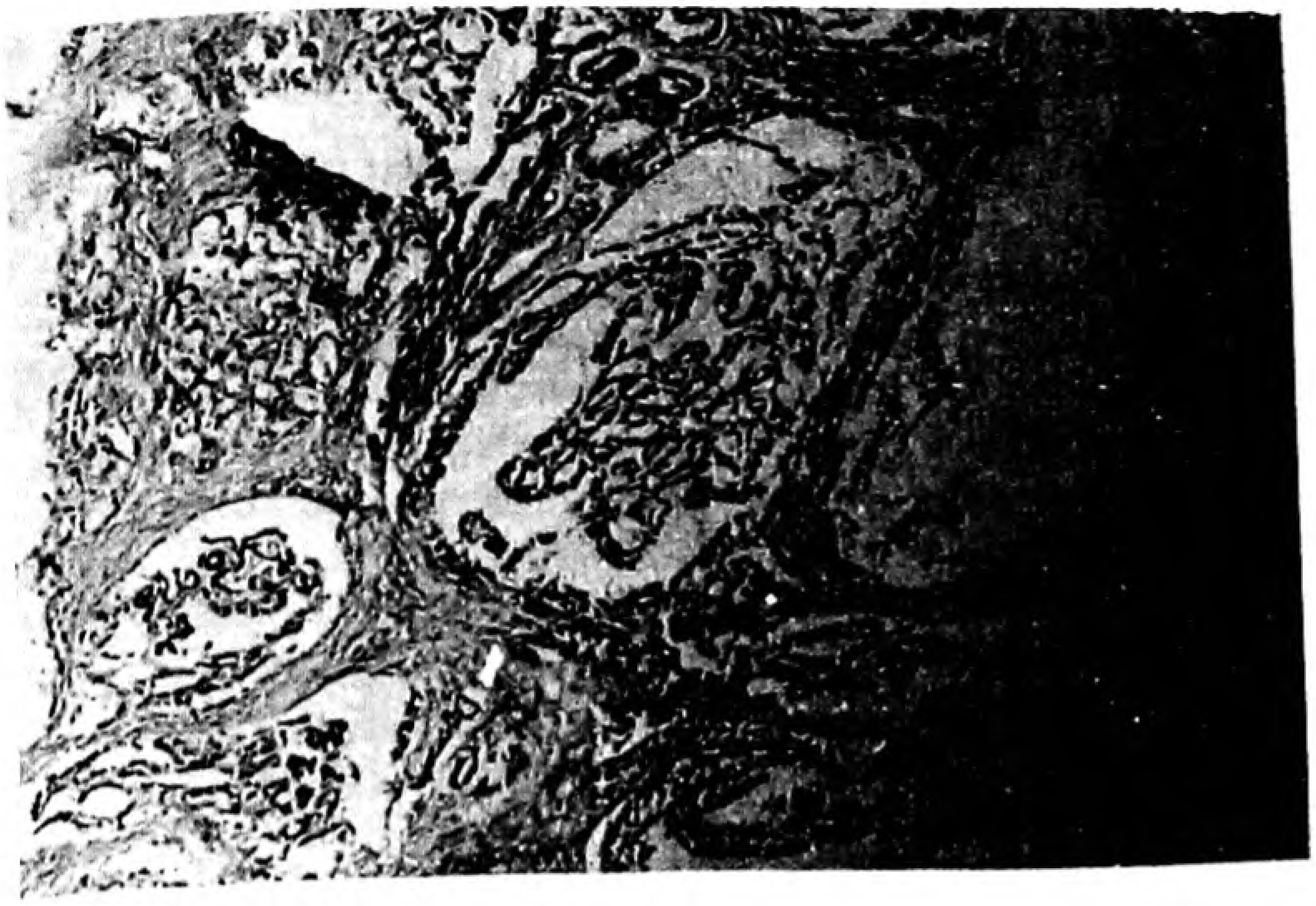

Figure 1

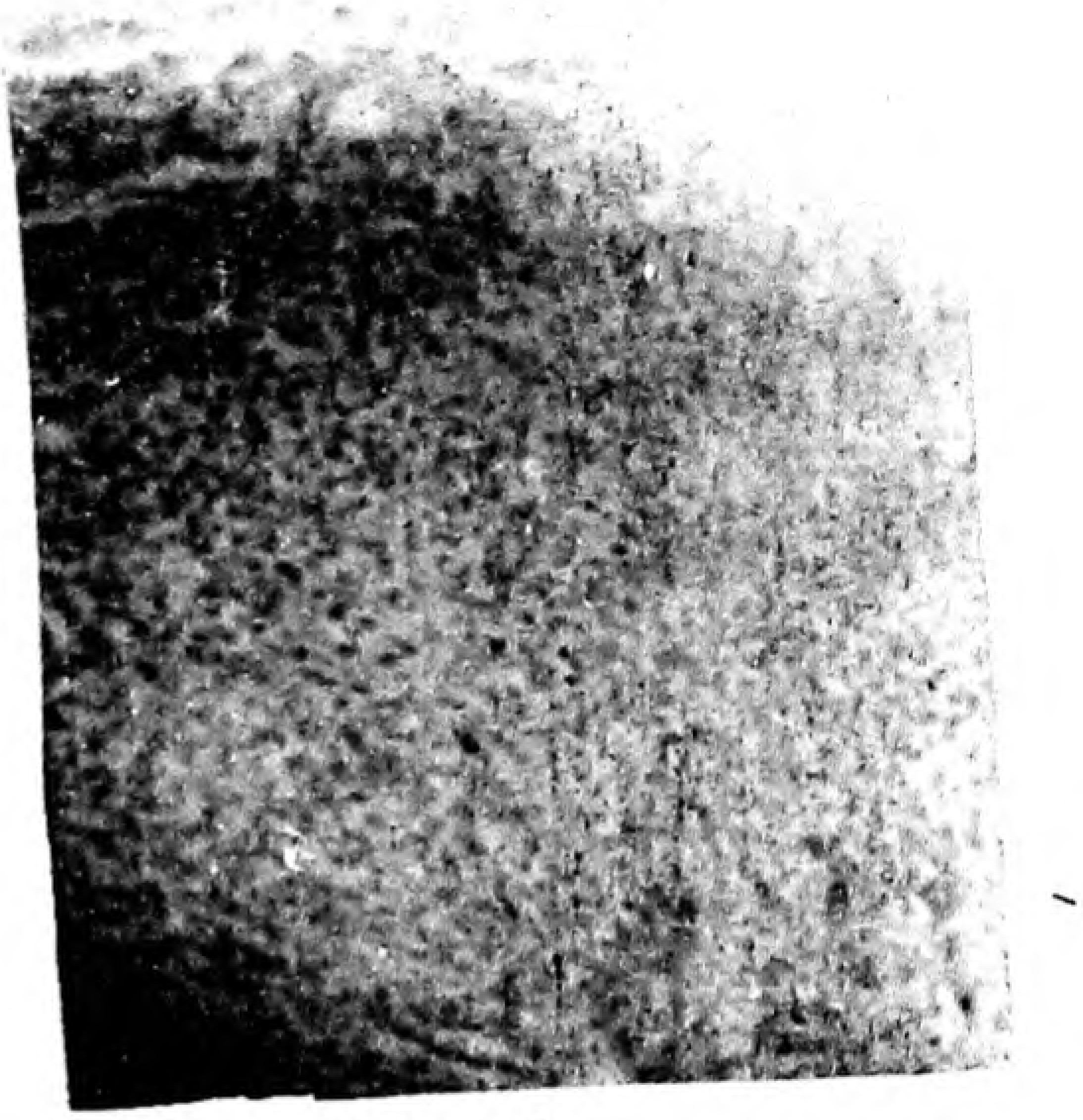

Figure 2

Table-III: Showing the age distribution in relation to the morphological types of gastric carcinoma

	Intestinal type		Diffuse type		Colloid Ca.	
Age distribution	No.	%age	No.	%age	No.	%age
11-20	1	0.21	-	-	-	-
21-30	5	1.03	5	2.50	-	-
31-40	46	9.50	20	10.00	2	3.70
41-50	250	51.65	104	52.00	20	37.00
51-60	160	33.06	62	31.00	23	42.60
> 60	22	4.55	9	4.50	9	16.70
Total	484	100.00	200	100.00	54	100.00

Table-IV:Showing the site distribution of gastric carcinoma.

S.No.	Site	No.	Percentage
01.	G.E. Junction	170	23.00
02.	Body	214	29.00
03.	Antrum & Pylorus	354	48.00
	Total	738	100.00

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Treatment of adenocarcinoma of gastro-oesophageal junction with chemoradiotherapy

Mushtaq A. M.D.; Sheikh Aejaz Aziz D.M.; Gul Mohammad Bhat M.D.; Banday Manzoor Ahmad M.D.; M.Y. Kharadi M.D.

Abstract: *From July 1992 to June 1996, 36 patients with performance score of 1 and 2 and age less than 65 years, who had localized,unresectable adenocarcinoma of gastro-oesophageal junction were treated with concurrent chemoradiation.*

Patients received radiation therapy 4000 cGYs over 4 weeks by two parallel opposed anterior and posterior fields and chemotherapy consisting of 5-Flurouracil (5Fu) 1gm/m²/24 hrs as continuous infusion over 96 hrs starting on day 2 and Mitomycin C (MMC) 6mg/m2 given as bolus intervals. Thirty two patients completed more than 2 courses of chemotherapy. The range of followup was 4 months to 36 months. Four patients were lost to followup. Of the 32 evaluable patients 30 had relief of dysphagia at the end of treatment and 24 patients continued to be dysphagia free till death. The median survival was 18 months range (4-36 months). Fourteen survived dysphagia free for more than 1 year. The treatment was well tolerated. Ten had mild oesophagitis and 4 had stomatitis. A fall in leucocyte count that necessitated reduction in the dosage of MMC by 25% occured in 4 patients during second or subsequent chemotherapeutic courses.

Our preliminary observations suggest that chemoradiation is an effective and well tolerated therapy with the aim of prolonging the dysphagia free interval for inoperable adenocarcinoma of GE junction.

Key words: *Chemoradiotherapy, GE Junction.*

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Introduction

Oesophageal cancer is the most common cancer in Kashmir (India) with incidence of 43.6 and 27.9/100,000 male and female population respectively[1]. Whereas squamous cell carcinoma is the common tumour affecting oesophagus, adenocarcinoma of oesosphagus and gastroesophageal junction (G.E. junction) is unusual variant of oesophageal cancer comprising between 0.2 and 15 percent[2].

The prognosis of oesophageal cancer continues to be poor with 5 year survival less than 10 percent and only 20 percent live at 2 years[3]. Surgery is the mainstay of treatment for patients with adenocarcinoma of G.E. Junction, however results with surgery continue to be grim with reported 5 years survival of 8 percent[4]. The presence of locally advanced disease at presentation is the main cause of failure with surgical treatment for adenocarcinoma of G.E. junction. In addition old age, low nutritional status and poor cardiovascular status compound the problems for surgical treatment. Thus treatment failure with surgery resulting in median survival of less than one year with reported operative mortality of 7% is multifactorial[5].

Adenocarcinomas are traditionally considered as relatively radioresistant tumours, however, it has been observed that oesophageal adenocardinoma is radioresponsive tumour[6,7]. The addition of chemotherapy with 5-Fluorouracil (5-Fu) and mitomycin C (MMC) to radiotherapy has been reported to enhance tumour control[8]. Our earlier experience with chemoradiotherapy as a non surgical primary method of treatment for squamous cell carcinoma of oesophagus with favourable results has prompted us to carry out this protocol in adenocarcinoma of G.E. junction[9] as similar tumour responsiveness has been observed in both squamous cell carcinoma and adenocarcinoma of oesophagus[10,11].

Overall survival in oesophageal cancer has not changed with various modalities of treatment including surgery, radiotherapy and chemotherapy used alone or in combination, therefore, the main aim of treatment remains relief of dysphagia with minimal treatment related morbidity. Chemoradiotherapy is emerging as a

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alternative to surgery atleast for those patients who are inoperable or who refuse surgery. In this study, we report our experience in 36 patients with adenocarcinoma of G.E. junction treated with 5Fu plus MMC combined with radiotherapy.

Material and Methods

36 patients with adenocarcinoma of J.E. junction were treated with combined protocol of chemoradiotherapy from July 1992 to June 1996. Patients characteristics are shown in table I. Patients were required to have biopsy-proven adenocarcinoma of G.E. junction with no evidence of gastric fundus tumour. In case of extension of tumour to gastric cardia, bulk of tumour had to be within the oesophagus. All patients with age less than 65 years and performance status on WHO scale less than 3 were included in the study. The patients with impaired renal functions were excluded from the study group. Initial evaluation included history, physical examination, X-ray chest, complete haematological and biochemical blood tests and ultrasound abdomen. Extent of the primary disease was evaluated by barium swallow and endoscopy measuring length of the lesion. CT scan of thorax and upper abdomen was performed to know the metastasis in mediastinum and celiac areas.

All patients were treated with external radiation using two parallel opposed field with Cobalt-60 to the total radiation dose of 4000 CGy in 20 fractions over 4 weeks. The radiation portals included known visible tumour with 5 cm of normal oesophagus on proximal end and coeliac nodes. No boost radiotherapy was given in any patient in view of advanced disease. Treatment plan is depicted in table 2.

Chemotherapy was started on day 2nd of radiation with 5-FU continuous infusion 1 gm/sq meter over 24 hours for 4 days. MMC 6mg per sq. meter was administered as a bolus injection on day 2nd. Four such chemotherapeutic courses were given at interval of 4 weeks. Blood counts were monitored weekly during Ist course of chemotherapy when it was combined with radiation and then before giving chemotherapy in subsequent courses. Twenty five percent reduction in dose of 5 FU was made in subsequent courses if the patient had developed grade III mucositis or persistent leukopenia with WBC count less than 2000 and thrombocytopenia with platelet count less than 75,000 persisting more than a week following chemotherapy courses. Nutrition was maintained with dietary suplements and in patients with grade III mucositis with parenteral hyperalimentation.

Results

Patients were assessed and reviewed 6 weeks after completion of the treatment. Local response to the treatment was assessed by endoscopy and barium swallow examination. Response to the treatment was recorded as per WHO criteria[12]. Complete response on endoscopy was confirmed by biopsy and brush cytology. Subjective response was determined by degree of relief of dyspahgia.

Out of 36 patients, 32 patients completed atleast 2 courses of chemotherapy in addition to radiation treatment and were evaluated. Eight had complete response and 14 had partial response whereas 10 patients had relief of dysphagia, although they were not fulfilling criteria of CR or PR as per WHO scale. Median time to remain dysphagia free was 14 moths in CR group and 6 moths in PR group with overall average response duration a:; 7 months.

Out of 32 evaluable patients 12 patients survived more than 2 years with overall median survival of 18 months and survival ranging from 4 months to 36 months.

Local recurrence was the commonest cause of treatment failure in 80%. Twelve patients developed liver metastasis.

Morbidity of Treatment

The treatment with chemoradiation was well tolerated. There was minimal haematological toxicity associated with the treatment, however gastrointestinal toxicity in the form of stomatitis and oesophagitis was seen in majority olf patients (40%) in 3rd week of radiation treatment. It was mild in nature and controlled with symptomatic treatment in 90 percent patients. In 4 patients it was severe and required interruption of the treatment and were put on parenteral alimentation.

Discussion

The results of treatment of oesophageal cancer including adenocarcinoma of GE junction continues to be poor with all modalities of treatment surgery, radiotherapy and chemotherapy applied alone or in combination.

Addition of simultaneous chemotherapy to radiotherapy has been shown to improve local control and reduce the recurrence in adenocarcinoma of the oesophagus and GE junction[7,13]. Contrary to the traditional view that adenocarcinomas are radioresistant tumours, Coia et al[8] reported that the adenocarcinoma of cardia are markedly sensitive to chemoradiation treatment when given synchronously. These reports were further confirmed by Gill et al[7].

`Surery has been regarded as mainstay treatment for adenocarcinoma of GE junction but majority of the patients are not amenable to surgical treatment as most of the patients present with advanced disease at presentation. There is high incidence of early spread to hepatic, para-aortic lymph node and distant metastasis[2,5] resulting in poor results of the surgical treatment[14]. In view of old age and poor cardio-respiratory status there is high operative mortality ranging between 7 to 20 percent[15,16]. Surgical bypass has also been advocated for adenocarcinoma of GE junction but has not proved effective treatment with significant morbidity and mortality[17,18]. Therefore, surgery should be reserved in only those patients who have early disease.

With the limited duration of life expectancy in these patients, the main aim of treatment remains relief of dysphagia with minimal treatment related mortality. In our study, the relief of dysphagia was achieved in almost all patients within 6 weeks after completion of radiation therapy and above all there was no significant treatment related morbidity or mortality except in 2 patients who were hospitalized for severe oesophagitis and recovered within one week following supportive treatment.

The results of radiotherapy alone in treatment of GE junction have not been sufficiently good with minimal impact on survival[19]. Similarly adenocarcinoma of GE junction is refractory to most of chemotherapeutic drug when given alone. All these data has led a number of investigators to use multimodality treatment in an attempt to improve local control and survival. Preoperative radiation followed by surgery has also been extensively used in adenocarcinoma variant of the oesophageal cancer also as in its sqamous counterparts, but its beneficial effect has not been confirmed by randomized trials and there is an additional substantial operative mortality[20]. Several trials have been conducted to use concurrent chemotherapy and radiation prior to attempt surgical resection. Though the preliminary results are encouraging but it should not be at the cost of increased treatment related morbidity and mortality[21]. Thus chemoradiation treatment as sole method of treatment has been attempted in various studies with promising results in adenocarcinoma of GE junction[7,8]. The addition of chemotherapy used concurrently with radiotherapy leads to better tumour regression due to radiosensitizing effect as reported by Coia et al[9]. In non-randomized trial John et al[10] found that the patient treated with radiotherapy alone achieved lower rate of tumour regression on endoscopy. It substantiates role of chemotherapy on tumour regression by enhancing the effect of chemotherapy. Two more courses of chemotherapy after the completion of synchronous chemoradiation is aimed to control systemic micrometastasis as advocated by Gill et al[7]. This study confirms the effectiveness of combined chemoradiation treatment using 5FU and MMC in adenocarcinoma of GE junction and is well tolerated. It should be offered in all patients with adenocarcinoma of GE junction atleast who are inoperable or who refuse surgery.

Table-I: Patient Characteristics.

Total No. of patients	36
Evaluable	32
Age (years)	
Range	40-60
Mean	52
Sex	
Males	22
Females	14
Performance status	
I	10
II	26

Table II: Treatment plan

Day	1 2 3 4 5	2930313233	6162636465	89 909293
Treatment Inj Mitomycin C (6mg/m2)	+	+	+	+
Inj. 5FU infusion (1gm/m2/ 24 hrs + (6mg/m2/24hrs)	+ + + +	+ + + +	+ + +	+ + + +
RT 200 cGY/ day 20 frs. (day 1-29	————			

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Therapeutic Splenectomy in Hereditary Spherocytosis

Fazal Q. Parray, MS.; Nazir A. Wani MS., FICS., FRCS.; Khursheed A. Wani MS; FICS.

***Abstract**: 15 patients with hereditary spherocytosis were subjected to therapeutic splenectomy in the department of General Surgery at Sher-i-Kashmir Institute of Medical Sciences, Srinagar from 1982 to 1995. This disease entity comprised of 14.70% of whole study group subjected to splenectomy for various hematological disorders. Male: female ratio was 1:1.4. The disease mainly involved the younger age group (mean age 18.60). The main indication for splenectomy in hereditary spherocytosis was anemia. All the patients were subjected to elective splenectomy.*

The response to splenectomy vis-a-vis hematological parameters was excellent. 86% patients showed a complete response; 7% showed a partial response and rest of 7% showed no response. Overall 93% patients were benefitted by the procedure. The morbidity was 13.33% and the mortality was 6.66%. The conclusion was that therapeutic splecectomy is the procedure of choice for treating patients of hereditary spherocytosis, provided that there is an excellent cooperation between a surgeon and a hematologist.

Key words: Splenectomy; Hemolytic ancumia; Hereditary Spherocytosis.

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Introduction

Hereditary spherocytosis is a type of congenital hemolytic anemia characterized by an intrinsic defect of the red-cell membrane. The defect results from deficiency in spectrin that is thought to be responsible for the shape, strength and reversible deformability of the red blood cells. The disease occurs primarily by autosomal dominant inheritance, and twenty to twenty five percent of cases appear sporadically (Wintrobe, 1990)[1].

The first total splenectomy for disease is attributed to Adriano-Zaccarallo in 1549, although it has been suggested that the excised viscus was an ovarian cyst. However, it was not until the mid of 19th century that the therapeutic splenectomies were performed for splenic enlargement[2]. In recent times, the role of splenectomhy in various hematoloical disorders like hereditary spherocytosis and idiopathic thrombocytopenic purpura has been widely applauded in most of the studies.[3] The optimum time to perform the operation for hereditary spherocytosis is in late childhood or early adolescence before liver changes have occurred.[2]

Material and Methods

The study includes 15 patients with "Hereditary spherocytosis" subjected to therapeutic splenectomy from 1982 to 1995 at Sher-i-Kashmir Institute of Medical Sciences, Srinagar (J&K), India in the department of Surgery. The cases were worked up, diagnosed and referred to our department mainly, by the department of Clinical Hematology.

Medical records of all the retrospective cases were reviewed. Pre-operative management included a detailed clinical examination, hematological and coagulation studies. All patients were subjected to pre-operative ultrasonography to find the status of spleen, and to rule out any associated cholelithiasis. Pre-operative hematological parameters showed Hb% of <8g in all the patients as shown in Table I.

Table I-Showing the hematological parameters in pre-operative period

Parameters	Range	No. of cases	Percentage
Anaemia	Hb<8g%	15	100
	Hb8-10g%	Nil	x

All patients were subjected to elective splenectomy under general anaesthesia by a left upper paramedian incision. After splenectomy a careful search for splenuculi was carried out in the region of tail of pancreas, along the splenic artery to its origin and in the gastrocolic omentum and the mesentry of small bowel.

Patients who were pre-operatively on steriods, hydrocortisone was used and rappered for 48-72 hours in post-operative period. A preset routine was followed for taking blood samples on day "Zero", day "3" and day "7" in the post-operative period and then Ist month,

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[illegible] following [illegible] month [illegible]

[illegible] count and platelet [illegible] most of the studies [illegible]

[illegible] described [illegible]

[illegible] Platelet Count [illegible]

[illegible] reports [illegible] Other studies [illegible]

[illegible] point of Horan and Cole [illegible]

[illegible] Leukocyte count [illegible] or above [illegible] advent of safe [illegible] and broad [illegible]

[illegible] mortality following [illegible]

[illegible] Erak [illegible]

[illegible] idiopathic thrombocytopenic [illegible]

[illegible] the mean age [illegible] disease [illegible]

[illegible] study group of 102 patients [illegible]

[illegible] 3.7 [illegible] 2g%) with [illegible]

[illegible] cholelithiasis [illegible]

[illegible] study (1981)[4] [illegible]

[illegible] The frequency [illegible]

[illegible] could [illegible]

conferring the lasting cure for jaundice and anemia. However, the chance of splenectomy conferring cure or improvement in hematological disorders must be balanced against the cost in terms of post-operative mortality and morbidity including late post-splenectomy fulminant infections.

Table II- Showing "Response to Splenectomy"

Disease	Total no. of patients	Response	Percentage
Hereditary Spherocytosis	14	Complete (CR)	12 pts. 85.71
		Partial (PR)	01 pt. 7.14
		No response (NR)	01 pt. 7.14

Note: One patient died on the post-operative period, (note included in the table)

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C-Reactive Protein in CNS Infections in Children

Muzaffar Jan MD, DCH.; Wajid Ali MD.; Mushtaq Ahmad MD. MRCP.; A.S.Sethi MD.

Abstract: CNS infections are amongst the major cause of morbidity and mortality in children. For decreasing mortality and morbidity from these infections it is mandatory that they are diagnosed early and treated promptly.

In the present study Serum and Cerebrospinal fluid (CSF) C-Reactive protein (CRP) levels were studied in 70 cases. 20 cases served as control, 38 had Pyogenic meningitis, 4 had Tubercular meningitis, 3 had Aseptic meningitis and 5 had Encephalitis. Mean value of Serum and CSF CRP level in Pyogenic meningitis was 32.5 ml/l and 20.5 mg/l respectively. Mean value of serum CRP in Tubercular meningitis was 9 mg/l while as CSF CRP in tubercular meningitis was normal. Serum and CSF CRP levels in case of Aseptic meningits and Encephalitis were normal. Serial estimation of Serum and CSF CRP levels revealed that CRP levels rapidly returned to normal with clinical recovery and response to therapy. However these patients who showed no response to therapy and who developed sequelae, continued to have raised Serum and CSF CRP levels. Measurement of CRP is therefore an excellent parameter in diagnosis, differentiation and prognosis of C.N.S. infections.

Key words: C-Reactive protein; Meningitis; Cerebrospinal fluid.

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Introduction

Central Nervous System infections are amongst the major cause of morbidity and mortality in children. Past four decades have seen a considerable fall in the mortality from C.N.S infections. However morbidity still ranks high especially so in the developing countries.[1]

For decreasing mortality and morbidity from CNS infections it is mandatory that they are diagnosed early and treated promptly. Assessment of CRP in serum and CSF is a rapid and simple technique which helps in diagnosing various CNS infections as well as in differentiating between them.[2,3,4,5]

The present study investigates the value of serial CRP measurement in serum and CSF for diagnosis, differentiation and prognosis of C.N.S. infections.

Material and Methods

A total of seventy cases ranging from 3 months to 14 years of age were studied in Government Children Hospital, Srinagar for a period of 1 year. Out of these 20 served as controls, 38 had pyogenic meningitis, 4 had tubercular meningitis, 3 had viral meningitis and 5 had encephalitis. Vinken Bruyn criteria were applied for the clinical diagnosis of C.N.S. infections.[6]

Patients in control group were admitted for diseases other than those which could have altered CRP in blood and C.S.F. 50% of these cases were males and 50% females. Investigations done in the cases were CBC, ESR, X-ray Chest, Sputum and/or gastric aspirate for AFB (wherever felt necessary). Blood culture, CSF analysis on day 1, day 4 and day 11 of presentation, C.S.F. culture, Mantoux and or BCG test, Serum CRP estimation on day 1, and day 11 and CSF CRP estimation on day 1, day 4 and day 11.

CRP estimation was done semiquantitatively by rapitex (R), CRP, a late agglutination kit[7], a concentration of more than 6 mg per litre was taken as positive.

Results

Out of the 33 patients of pyogenic meningitis 16 (42%) had positive blood culture, whereas 15 (39.5%) had positive CSF culture. Organisms recovered from blood culture are Nisseria meningitis group A in 8 cases. H. Influenzae in 3 cases, Pneumococcus in 3 cases, Streptococcus in 1 case and Staph. aureus in 1 case.

Of all the cases of pyogenic meningitis Gram. stain of C.S.F. was positive in only 7 (18.4%) cases.

The serum and CSF CRP was negative (i.e. less than 6mg per litre) in the control group.

Comparison of the day 1 serum CRP levels reveal that CRP rises to significant levels in all cases of pyogenic meningitis and 75% cases of tubercular

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meningitis. However, the rise being higher in pyogenic meningitis (mean 32.5mg/l) than in tubercular meningitis (mean 9mg/l). Day 1 serum CRP was negative (less than 6 mg/l) in all the cases of viral meningitis and encephalitis. The difference between the pyogenic meningitis (where 94.7%) cases had serum C.R.P. more than 12 mg/l and non-pyogenic group (tubercular meningitis, viral meningitis, encephalitis, controls) where all the cases had serum C.R.P. less than 12mg/l was statistically significant. (P value less than 0.01).

Comparison of day I C.S.F. C.R.P. levels reveal that 94.7% cases of pyogenic meningitis have raised CSF CRP. The mean value being 20.5 mg/l. Remaining cases of pyogenic meningitis and all cases of tubercular meningitis, viral meningitis and encephalitis had a normal C.R.P. levels. The difference between the pyogenic meningitis and non-Pyogenic group was statistically significant. P value less than 0.01.

Serial estimation of C.R.P. has shown a considerable fall of C.R.P. levels with clinical recovery and treatment. In Pyogenic Meningitis the serum C.R.P. level returns to normal by day 4 in most cases and in 94.8% cases by day 11. However in tubercular meningitis the serum CRP level continues to remain elevated by day 4 and returns to normal only by day 11.

Comparing serial CSF CRP levels, in pyogenic meningitis the CSF CRP falls dramatically with clinical recovery, becoming negative in 2nd (day 4) CSF examination in most cases and in 3rd (day 11) CSF examination in 89.5% cases.

The serial estimation of CRP in serum and CSF revealed decrease in levels with clinical recovery. However in 2 patients of pyogenic meningitis who did not show clinical recovery with proper therapy, serum and CSF CRP levels continued to remain elevated or increased further.

Two (5.2%) cases of pyogenic meningitis developed sequelae. One developed hemiplegia and the other one hydrocephalus. In both the cases the serum and CSF CRP levels continued to remain elevated during first week of therapy.

One case with tubercular meningitis developed 7th nerve palsy. In this case the serum CRP level remained elevated during the first week of therapy.

Discussion

C.N.S. infections are common entities that confront us in day to day practice, their diagnosis mostly depend on CSF examination. There are many situations where etiological diagnosis becomes namely in partially treated pyogenic meningitis and tubercular meningitis, both can present with the same clinical and CSF picture. Viral and tubercular meningitis at some stage have same CSF picture. Viral meningitis may present with polymorphonuclear leucocytosis in early stages and may need differentiation from early pyogenic meningitis.

In present study serum CRP was found to be raised in 100% cases of pyogenic meningitis and 75% cases of tubercular meningitis. However the rise being far more high in pyogenic meningitis than in tubercular meningitis. Similar were the observations of Harish, Sable and Hanson, Peltola, Klarke and Cost.[2,5,8,9]

Normal serum CRP levels were found in patients with viral meningitis, encephalitis and in control group. Similar were the observations of Sharma et al.[10]

CRP levels in CSF were raised in 94.7% cases of pyogenic meningitis. The sensitiviy of detecting CRP in CSF of patients with pyogenic meningitis was 0.94 and the specificity was 1. Similar were the observations of Singh et al & Gupta et al.[3,11]

CSF CRP was normal in cases of tubercular meningitis, viral meningitis, encephalitis and in control group. Similar were the observations of Gupta et al and Sharma et al.

Serial estimation of CRP revealed decrease in levels with clinical recovery. However in cases of pyogenic meningitis who did not respond to antibiotics, both serum and CSF, CRP levels remained elevated or even increased further returning back to normal only after change in antibiotics and clinical recovery.

Sabel and Hansen observed that period of increased CRP was closely related to the risk of recurrence of infection. We feel in addition to this, persistently elevated CRP levels in serum and CSF suggest persistence of infections.

Two cases of pyogenic meningitis and one case of tubercular meningitis who developed sequelae showed elevated CRP levels during first week of therapy. Similar were observations of Singh et al.[12]

Conclusion

Measurements of serum and CSF CRP not only helps in early diagnosis of various CNS infections but also helps us to differentiate between them. Decreasing serum and CSF CRP levels in serial estimation means gradual recovery. While as persistent high levels or increasing levels reflect either persistence of infections or recovery with sequelae.

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Exchange transfusion in Neonatal Jaundice and its outcome

Mushtaq Ahmad MD; Wajid Ali MD; Muzaffar Jan MD. DCH; G. Qadir B.Sc; Masood ul-Hassan MD.

Introduction : *Neonatal jaundice is a common medical emergency in the Neonatal Intensive Care Units, because bilirubin is a potentially neurotoxic substance. The limited ability of a neonate to metabolise unconjugated bilirubin predisposes the baby to the risk of bilirubin encephalopathy and its consequent long term sequalae. Appropriate management of neonatal jaundice is a paramount importance, especially when bilirubin, even in physiological ranges, may cause permanent neuronal injury[1]. Exchange transfusion, developed fifty years back by Diamond[2], is the corner stone to prevent the permanent neuronal damage, the Kernicterus. Present study was undertaken to analyse the causes of neonatal hyperbilirubinemia, needing exchange transfusion and its outcome.*

Key words:

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Subjects and Methods

Out of 647 admission to the Neonatal Intensive Care Unit of the Sher-i-Kashmir Institute of Medical Sciences, Srinagar, from Ist July 1996 over a period of one year, 70 babies underwent exchange transfusion. This hospital is a level three referral hospital in the Kashmir valley and the referrals were from the Obstetric Unit of the Community Medicine Deptt. of this Institute, 500 bedded Lala Ded Memorial Women's Hospital of Medical College, Srinagar and the various district headquarter hospitals of the valley.

Detailed antenatal, natal, postnatal and family history were taken and detailed examination of the baby done. Blood grouping and Rh. typing of mother and baby were done. Haemogram, Red Blood Cell morphology, Reticulocyte count, Direct Coomb's test, Blood culture sensitivity, G6PD estimation (in Idiopathic type) of the babies was done. Kidney function tests, Blood Sugar, Serum calcium Na^+/K^+ Arterial blood gas and serum bilirubin were taken pre and post exchange. Bilirubin estimation was repeated 2 hours, 6 hours, 12 hours and 24 hours post-exchange. Bilirubin estimation was made by Polymac F-4 Microprocessor. Cockington charts were used as a guideline for the therapeutic intervention of phototherpy and exchange transfusion.[3]

Babies were divided into two groups (i) group I- wt<2.5 kgs (ii) group II- wt.>2.5 kgs. In all cases double volume exchange transfusion was done using disposable (Vygon) exchange sets and citrate phosphate dextrose (CPD) fresh blood phototherapy was used pre and post exchange. Babies were given nothing orally for 24 hours or till umbilical catheter was removed.

Patients were discharged at packed cell volume (PCV) above 40%, weight more than 1.8 kgs, Serum bilirubin below photozone (3) and sucking well at breast or bottle.

Results

Out of 647 admissions, 115 (17.77%) were having jaundice. Out of these 70 patients (10.81%) of total admissions and 60.86% of all jaundice cases needed exchange transfusion. Full term babies (group I) were 18 (25.71%) and preterm/low birth weight (group II) were 52 (74.29%. Out of low birth weight babies 24 (34.28%) weighed 2001-2500 gm, 13(18,57%) weighed 1501-2000 gm and 15 (21.42%) les than 1500 gms. 45(64.28%) babies were male and 25(35.72%) were females. Total serum bilirubin (TSB) was more than 20 mg% in 40 (57.15%) babies and less than 20 mg% in 30(42.86%) babies. In 60(85.72%) babies exchange transfusion was done through umbilical vein and in 10(14.28%) babies branchial artery and antecubtal vein were used for exchange transfusion (ET) due to difficult umbilical vein catheterisation and age more than one week. 47(67.14%) babies needed an exchange transfusion (ET). 12(17.14%) needed two ETs, 8(11.42%) babies required three ETs& 3(4.28%) babies underwent four exchange transfusions.

Commonest cause of Neonatal Jaundice needing one or more ET was ABO Hemolytic disease of newborn (ABOHDN) 35.71% followed by Idiopathic group (no cause could be ascertained). 21.42% Rh Hemolytic

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disease of newborn (Rh HDN), 17.14% Birth Asphyxia, 8.57% septecemia, 7.14% Polycythemia, 4.28% extravasation of blood (Sub aponeurotic bleed) 2.85% and oxytocin given to mother 2.85% (Table I). Minor blood groups, pyruvate kinase estimation were not performed.

Complications were divided into immediate and Delayed in both groups I and II (weight <2.5 kgs and >2.5 kgs). Immediate or procedure related complications were those occuring during or within six hours after the exchange transfusion.

Immediate complications were cardiorespiratory arrest. Tachycardia (Heart rate>180/mts). Bradycardia (HR<100/min) and difficult umbilical cateterisation. Delayed complications included anemia, congestive cardiac failure, Sepsis (blood culture positive), Pre-NEC (distension abdomen, occult blood in stools with a normal Abdomenal x-ray) and Electrolyte disturbance (Hyponatremia).

In group I cardiorespiratory arrest during ET occured in 1(1.2%) baby, who also had acidosis and birth asphyxia and was weighing 1.5 kgs. He was ventilated and expired after 24 hrs. Tachycardia was seen in 2 (2.85%), bradycardia in 4(5.71%), difficult umbilical catheterisation in 6(8.57%), anemia in 10(14.28%) congestive cardiac failure in 1(1.42%), pre-NEC in 4(5.71%) Hyponatremia in 2 (2.85%) and sepsis in 4(5.71%) babies. In group II cardiorespiratory arrest occured in 1(1.42%) baby who had hydrops, was ventilated and survived. Tachycardia occured i8n 2 (2.85%), bradycardia in 2(2.85%), difficult umbilical catheterisation in 4 (5.71%), anaemia in 5(7.14%), CCF in 1(1.42%), pre-NEC in 1(1.42%), Hyponatremia in 2(2.85%) and sepsis in 2(2.85%)) (Table II).

Discussion:

The most common cause for exchange transfusion in our study was ABOHDN (35.71%) as has been seen by some other workers[4]. Exchange transfusion in Rh HDN is coming down due to anti-D prophylaxis, smaller family size and early phototherapy. Regular use of tetanus toxoid especially during last trimester of pregnancy increases the risk of ABOHDN by virtue of increase in anti-A or anti-B titres probably due to presence of group specific substance in the culture medium.[5]

Second common cause in this study was Idiopathic (21.42%). Some workers have found Idiopathic group as indication for exchange transfusion with a figure of 21.5-48.0%[6]. Rh HDNwas a cause for exchange transufsion in 17.14% cases in this study. Maximum number of exchange transfusion were done for Rh. isoimmunisation, sepsis and G6PD deficiency by some

Table I

Cause of jaundice needing exchange transfusion

Cause	No.	%
ABO Hemolytic disease of newborn	25	35.71
Idiopathic	15	21.42
Rh Hemolytic disease of newborn	12	17.14
Birth asphyxia	6	8.57
Septicemia	5	7.14
Polycythemia	3	4.28
Extravasation	2	2.85
Oxytoxin to mother	2	2.85
	70	100%

Table 2

Complications of exchange transfusion

Complication	Group I (Wt.<2.5 kgs)	Group II (Wt.>2.5 kgs)
Immediate		
Cardiorespiratory arrest	1(1.42%)	1(1.42%)
Tachycardia (HR 180)	2(2.85%)	2(2.85%)
Bradycardia (HR 100)	4(5.71%)	2(2.85%)
Difficult umbilical catheterisation	6(8.57%)	4(5.71%)
Delayed		
Anemia (PCV<40%)	10(14.28%)	5(7.14%)
Sepsis (culture proved)	4(5.71%)	2(2.85%)
Pre-NEC	4(5.71%)	1(1.42%)
Hyponatremia	2(2.85%)	2(2.85%)
Congestive cardiac failure	1(1.42%)	1(1.42%)

HR: Heart Rate
PCV: Packed Cell Volume
NEC: Necrotising Enterocolitis

workers[1].

Asphyxia was a cause for exchange transfusion in 8.57%, septicemia in 7.14%, Polycythemia in 4.28%, Subaponeurotic bleed in 2.85% and oxytocin given to mother in 2.85% in this study.

Birth asphyxia depresses liver functions and increases the permeability of nerve cells. Oxytocin accentuates jaundice by decreasing haptoglobin and increasing plasma LDH like activity and further the vasopressin like activity of oxytocin stimulates water and electrolyte transport across red cell membrane resulting in hemolysis. Asphyxia neonatorum is known to increase the risk for developing Kernicterus. A restricted use of oxytocin for labour induction and maternal analgesia and anaesthesia to be kept to bare minimum to avoid respiratory depression in newborn is suggested[4]. (Septicemia is an important cause of jaundice needing exchange transfusion which could be reduced by using aseptic procedures).

In prematurity/LBW immaturity of liver functions hypoglycemia, acidosis, hypothermia and hypoxia are known contributory factors. Male gender in this study was 64.28%, is a strong risk factor for pathological jaundice[6].

More than one exchange was needed in 32.85% babies in our study, which is in comparison to 21.8% in other Indian studies [4,7] on higher side.

Procedure related mortality has been defined as unexplained death during or within six hours of exchange transfusion[8]. In present study, no death was reported within six hours of exchange transfusion as is seen in other studies[1,9]. Mortality of 1-4%[10] and 3.2%[4] has been reported by other Indian studies.

Post exchange late complications were anemia (packed cell volume-PCV-less than 40%) mainly and sepsis in present study as has been seen by others[4,11,12]. Post exchange anemia can be reduced by using voluntary donors with high hematocrits as against professional donors and by topping up a few mili-litres of extra blood at the end of each exchange transfusion. Septicemia can be prevented by strict aseptic precautions and by using disposable exchange transfusion sets. Ten out of seventy exchange transfusions were performed through peripheral route. We used brachial artery and antecubetal vein without any complication.

Kernicterus giving permanent neurological disability to the child is the complication of neonatal hyperbilirubinemia, which can be prevented by timely interventiuon using exchange transfusion which is a safe procedure.

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Physical Growth Among Adolescent Kashmiri girls from Elite Class

Bhat Imtiyaz Ali MD.; Abida Ahmad MD.; Khan Neelofar MD.;

Abstract: *A cross-sectional study on 437 normal healthy Kashmiri girls belonging to prestigious schools (admitting girls mainly from Elite Social Class) in the age of 5-15 years has been conducted to obtain physical growth characteristics. The growth measurements have been obtained in accordance with recommended standard procedure.*

The girls were both heavier and tall in comparison to ICMR standards and values corresponded to 50th centile NCHS standard upto 10th year of age beyond which the girls were following around 25th centile NCHS values for both weight and height till 14 years. The peak velocity for height was attained earlier at around 10-11 years and for weight one year latter i.e. 11-12 years of age. Though the mean height and weight values and the growth velocity in the present study were comparable to Indian well to do girls and other North Indian Studies yet the values were far below the British and American adolescent girl standards.

Key words: *Growth, Adolescence, Weight and Height, peak velocity.*

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Introduction

The nature of children's growth and physical development mainly depends upon nutritional status and environmental conditions which interrelate with other socio-economics, biophysiological, demographic and physical environments.[1] For interpreting growth, National Centre for Health Statistics (NCHS) standards in anthropometry are the ones thought to represent normal growth and widely used including India. Although this standard is used internationally, WHO has cautioned for its use beyond 10 years of age because of wide difference in the time onset of puberty among different population. Study on affluent girls (9-18 years) drawn from four regions of country, (Delhi, Mumbai, Calcutta and Coimbatore) showed considerable regional difference with respect of patterns of growth among affluent adolescent girls. The affluent girls of Delhi showed best growth performance and were as tall as American girls (NCHS) at all ages till their 11th and 12th year. However, after 12th year, growth of Indian girls did not keep pace with that of American counterparts.[2] This implies that data with regard to growth and development from a healthy normal children, with least likelihood of constraints imposed from malnutrition and infection, need to be collected and local standards developed.

In the light of above knowledge and the fact that girl child in this part of country (Kashmir valley) is living in an different topographic and socio-cultural background with no such information on growth of girls from upper socioeconomic class available; the present study was carried out and is presented.

Material and Methods

A cross sectional study from three prestigeous public schools (Convent, Burn Hall and Mallanson Girls School) of the valley catering to the educational needs of elite of the society has been conducted. A moderate sample of 437 from 5 years upto 15 years was obtained by purpostive random sampling technique of which only 379 girls had complete information in all respects for analysis. Children from these schools with no signs or symptoms of constraints likely to interfere with growth were included. Exact date of brith was verified from school registers and age was rounded upto nearest years. Measurements of physical growth characteristics were carried out according to methods described by Tanner & Jelliffee.[3,4] Weight was taken by using UNICEF (platform) beam balance measuring to the nearest of 0.1 kg. Zero error was corrected each day before actual weighing. Height was recorded to the nearest of 0.1cm by stadiometer. MAC was obtained at the mid-point of upper left arm kept in semiflexed position at elbow. All the observations were recorded by one author fully trained for the job between 10 to 1 p.m. Head and chest circumference were obtained as described by Jelliffee and Jelliffee.[4]

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Observations

Majority of parents in studied sample belonged to professional class (52%) or business class (28.5%) with an average month income between Rs. 8000/- to Rs. 10,000/- per month. About 75% girls were having both parents literate. All the girls belonged to urban locality.

Table-I shows that mean weight of girls at 5 years was 17.17+2.23 Kgs with a gradual increase upto 9 years of age and then a sudden increase at 10th year from 25.17+3.88 kgs to 30.33+7.21 kgs reaching finally to 43.7+2.05 kgs by 13th years and 47.16+3.62 kgs by 15th uear. The mean height of girls at 5 years was 113+7.30 cms showing gradual increase upto 9th year and thereafter a rapid increase between 10-13 years reaching from 136.04+4.04 cms to 154.06+3.21 cms. Mid arm circumference (MAC) was 15.6+1.42 cms at 5 year gradually increasing by 12-13 years and thereafter a sudden increase to 25.01+1.52 cms by 14 years of age. The head circumference was 48.47+2.08 cms at five years with almost a constant slow increase reaching to 54.81 cms by 15 years and chest circumference of 52.85+3.65 cms at 5 years reaching to 62.82+3.11 cms at 9 years and 78.0+1.29 cms by 14 years. The BMI at 5 years was .138 increasing to .163 at 10 years and by 15 years it reached to .192.

Table-II shows a maximum gain of 18.57 kgs weight obtained between 10-13 years and a similar gain of 24.8 cms in height in the same age group. MAC shows a very minimal gain of 2.38 cms by 9 years of age and thereafter an increase of 3.0 cms by 13th year and another 5.01 cms by 15th year. An overall gain of 12.62 kgs in weight, 23.04 cms in height and 3.95 cms in MAC was observed between 5-10 years whereas it was 16.83 cms and 6.96 cms between 10-15 years. The maximum gain in height of 7.90 cms in the 11th year and 5.76 kgs in 12th year can also be observed (Table- III).

Discussion

The present study has shown that the data is quite comparable to other studies on well-to-do Indian children.[5,6] However, our girls were both tall and heavier once compared to national average (ICMR data)[7] and the girls were around 90th centile ICMR values showing thereby that only 10% of girls will be above our average values. It is pertinent to mention here that ICMR values have been computed mostly from lower socioeconomic group which constitutes majority of Indian community and these values represent growth of an average child and can not be considered as normal children . Also girls in the present study belong to a medically and socially protected elite group which presumably are wellfed also. Out girls were comparable in stature and weight to the 50th centile values of NCHS upto 10 years beyond which they lagged behind and were usually falling around 25th centile NCHS values upto 12th year (or 13th year). This pattern has already been reported for Indian well-to-do girls.[8] (Fig I & II).

The peak velocity (maximum growth) was achieved between 11-12 years for weight and 10-11 years for height in our girls. These findings are consistent with the observations of Sathyavathi et al and Agarwal et al.[9] The peak weight velocity of 5.76 kg/year and peak height velocity of 7.5 cms/year at 12th year and 11th year respectively is slighter better to Qamert et al[10] who reported maximum gain of 6.9 cms/year between 11-12 years for height and 4.5 kg/year at 12th year for weight.

In general there has been a gradual stature increase of 3 cms/year in pre-adolescent period (5-10 years) followed by almost double fold increase of 6.5 cms/year during adolescent period upto 13 years of age and thereafter negligible increase. Similarly weight of the girls has shown very slow increase of 1.5 kg/year in pre-adolescent period which jumps to around 5 kg/year during adolescent period. These findings are comparable to growth pattern of Varanasi girls as shows by Pereria et al.[12] However, the annual mean growth velocities are far below average of British & American children. The overall gain in the weight and stature between 10-15 years was 16.83 Kgs and 20.34 cms respectively in our study which is better to 13.0 kg and 17.5 cms increase observed among urban girls by Sathayvati et al.[10] However, these values are far below the weight gain records of 19.61 kgs and 23 cms for American girls and 23.3 kgs and 20.0 cms for British girls. The better BMI value at 5 years in this study shows that girls did not star with much insult at 5th year.

The mean values of mid arm circumference (MAC) from 9th year to 15th year almost comparable to Varanasi girls[11] and the peak increase of 2.1 cm/year is seen at 12th year. Overall increase of 6.96 cms between 10-15 years of age in our girls is definitely better to Varanasi girls. Similarly chest circumference (CC) values were almost comparable and an increase of 4.16 cms at 12 years is the maximum increase in our study which is similar to 4.0 cms/year at 11-12 years of age shown by Periara et al.[12] However, among American it is earlier i.e. 10-11 years and between 12-14 years among Delhi girls.

Table-I: Physical growth characteristics of girls from elite Class.

Age group BMI(Kg)	Anthropometric Parameters Weight (Kg)	Height (cms)	MAC (cms)		H.C. (cms)	C.C.
5	17.71 ±2.23	113.0 ±7.30	15.66 ±1.42	48.47 ±2.08	52.85 ±3.65	0.138
6	19.29 ±2.71	116.82 ±7.70	15.94 ±2.7	49.11 ±2.34	55.05 ±3.86	0.141
7	22.04 ±1.23	120.52 ±7.70	117.15 ±2.7	51.94 ±2.34	58.10 ±3.86	0.151
8	24.42 ±0.78	124.83 ±3.57	18.0 ±1.63	52.94 ±2.34	60.14 ±3.60	0.156
9.	25.17 ±3.88	128.14 ±5.74	18.0 ±1.63	52.46 ±3.28	62.82 ±3.11	0.153
10	30.33 ±7.99	136.04 ±4.04	19.61 ±3.22	53.87 ±0.67	66.14 ±3.22	0.163
11	36.09 ±7.99	142.57 ±4.85	20.46 ±4.22	54.52 ±2.01	68.52 ±4.11	0.177
12	40.12 ±6.82	148.75 ±5.61	21.56 ±3.03	54.40 ±1.04	72.68 ±4.81	0.181
13.	43.74 ±2.05	154.06 ±3.21	21.78 ±1.19	53.90 ±1.77	74.59 ±4.68	0.184
14.	45.85 ±1.96	155.28 ±4.30	23.01 ±1.52	54.31 ±1.68	78.0 1.29	0.190
15.	47.16 ±3.62	156.38 ±6.71	23.57 ±0.78	54.81 ±1.31	78.66 ±3.33	0.192

Table-II: Anthropometric increment at different age groups.

Age group (cms)	Weight (Kg)	Ht. (cms)	M A C
5-10	12.62	23.04	3.95
10-15	16.83	20.34	6.96
Overall	29.45	43.38	

Table-III Increase in height, weight & MAC by age.

		Increase/Year	
Age groups	Weight (Kg/year)	Height (cms/year)	MAC (cms/year)
5-6	1.58	3.82	0.28
6-7	2.85	3.70	1.21
7-8	2.38	4.31	0.85
8-9	0.75	3.31	0.00
9-10	5.16	7.65	1.61
10-11	5.76	6.53	0.79
11-12	4.03	6.18	1.16
12-13	3.62	5.31	0.42
13-14	2.11	11.22	3.23
14-15	1.31	1.10	1.56

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Clinicopathological Study of Cysts in Ear, Nose, Throat Region

Nazir A. Khan MS; Abdul Majid MS.; Abdul Ahad MS.

Abstract : *The present study was carried out on 110 patients who came to ENT Department with various cystic lesions involving Ear, Nose and Throat region. 57.3% of the patients were males and rest females. Bulk of the cases of the study consisted of sebaceous cysts 30.9%, dermoid 27.2%, thyroglossal and branchial cyst 16.3% and 10.8% respectively. Swelling was the main presenting symtpom in all the cases except for vallecular and vocal cord cysts who presented with stridor and hoarseness of voice. Aspiration cytology and histopathological examination was carried out in all the accessible lesions to confirm the diagnosis. Surgical excision was employed as the standard method of treatment.*

Post operative complications like infection, haematoma and recurrence though encountered were insignificant.

Key words: ***Cystic lesions; Histopathology; Aspiration.***

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Introduction:

Though a number of studies have been carried out to study the incidence, specific clinical behaviour and pathology of different types of cysts in head and neck region, lack of enough literature and comprehensive study encompassing all types of cysts occuring in head and neck region prompted the present study.

Secondly our aim was to detail, incidence/pathology and clinical variation of cysts in head and neck region in relation to ENT practice.

From the available literature and various clinical studies it is evident that two types of cysts occur in head and neck region (1) congenital cyst, including (a) sequestartion dermoid, dermoid cysts of bridge of nose and midline of neck (b) Tubo-embroyonic cysts like thyroglossal cysts, (c) cysts of embryonic remanants like branchial cysts. (2) Acquired cysts include, implanation dermoid and mucous retention cysts due to trauma.

Diagnosis of these cysts is often made on clinical examination, but sometimes various investigative procedures, like nasopharyngoscopy, sinoscopy, direct laryngoscopy, aspiration cytology and radiological examination are mandatory.

Considering the various factors as frequency of their occurence, symptomatology, associated morbidity, if left untouched and recurrence that might follow the treatment, it becomes imperative to have a detailed scientific analysis of such patient, so that all the important factors are highlighted.

Material and Methods

This study was conducted on 110 patients who presented with cysts involving ear, nose and throat region in ENT department of SMHS Hospital Srinagar over a period of two years. Both male and female patients of all the age groups were taken up for the study. The patients were followed up for a period of 3-6 months. A detailed history was taken and patients presenting with fistulae, sinus, previous surgical intervention and recurrences were excluded from the study. Cases in which malignancy was suspected were likewise dropped from the study. A complete general physical and local examination of the lesion was carried out. ENT examination was carried out routinely on all the patients in this study.

Preliminary laboratory investigations deemed necessary before the administration of anaesthesia and surgery were carried out. Endoscopic examination e.g., nasopharyngoscopy, sinoscopy and direct laryngoscopy was carried out when indicated.

Radiological examination of the region involved was performed whenever necessary for diagnosis and to note extent of cystic lesion. This included contrast radiography of thyroglossal and branchial cysts. Thyroid scanning was done in case of thyroglossal cysts to know the location of functional thyroid tissue.

Fine needle aspiration was carried out in all the clinically acccessible cysts.

Most of the patients were admitted in hospital one day prior to surgery except where the cystic lesions were small, which were treated as out patients.

Surgical excision was carried out in all the cases

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except in two cases of vallecular cysts where marsupilisation was performed. Thyroglossal cysts were treated by classical Sistrunk's procedure. Histological examination of the excised tissue was carried out and diagnosis confirmed.

Post operatively patients were followed up over a period of 3 months to one year.

Observations:

During two years period 110 patients both males and females of all the age groups having cystic lesions in Ear, Nose and Throat region were taken up for study. Out of these patients there were 34 (30.9%) sebaceous, 30(27.2%) dermoid, 18(16.3%) thyroglossal, 12(10.8%) branchial, 3(2.7%) dentigenous, 2(1.8%) maxillary antral mucosal, cyst 2(1.8%) nasoalveolar, 2(1.8%) vocal cord, 2(1.8%) tonsillar, 2(1.8%) vallecular and 2(1.8%) dental cysts. Only one case (0.9%) of nasopalatine cyst presented during this study.

Majority of cases in the study presented with congenital cysts like, sebaceous, dermoid, thyroglossal and branchial cyst (94 cases). Of all the patients 63 (57.3%) were males and 47(42.7%) were females.

Only 5 cases of acquired cysts like mucous retention cysts involving lower lip were reported initially in the study but all of them were lost in the follow up and were therefore discarded from the present study.

The youngest patient in this series was a 1 year old male child having vallecular cyst and oldest patient was a 70 year male with a sebaceous cyst in the neck.

The sex distribution and the incidence of these lesions in different age groups is shown in the following table:

Type of cysts	Male	%age	Female	%age	Age range in years:
Sebaceous	20	58.8	14	41.2	10-70
Dermoid	16	53.3	14	46.7	11-28
Tyro glossal	10	55.5	8	44.5	18-50
Branchial	6	50	6	50	10-60
Dentigenous	3	100	-	-	15-25
Maxillary antral mucosal cyst	2	100	-	-	20-35
Nasoalveolar	-	-	2	100	19-37
Vocal cord	1	50	1	50	23-39
Tonsillar	1	50	1	50	45-55
Vallecular	1	50	1	50	1-2
Dental	2	100	-	-	40-50
Nasopalatine	-	-	1	100	18
Total	63	57.3	47	42.7	

The maximum number of patients presented with duration of symptoms between 6 months to 2 years. 7 cases each of sebaceous and thyroglossal, 3 cases of branchial and one case of dermoid cyst showed evidence of infection at the time of presentation.

2 cases (6.6%) of dermoid cysts showed stratified squamous epithelium without skin appendage while one case (3.3%) showed some areas of cuboidal epithelium in addition to skin appendages and stratified squamous epithelium.

12 cases (66.6%) of thyroglossal duct cyst exhibited pseudostratified columnar epithelial lining while as the remaining 11 cases (91.6%) had stratified squmous epithelium with lymphoid tissue present in 10 cases (83.3%).

Normal malpighian lining was seen in 2 cases of epidermoid cysts of vocal cords, while as 2 cases of dental cysts showed patches of squamous metaplasia in addition to ciliated columnar epithelium.

The rate of post operative infection was higher (14.7%) in sebaceous cysts as compared to thyroglossal (11.1%) and branchial cysts (8.3%), thyroglossal cysts showed a recurrence rate of 5.5% as compared to branchial cysts 8.3% and sebaceous cysts 8.8%.

Discussion:

Sebaceous, thyroglossal and dermoid cysts showed male preponderance, but no sex difference was observed in branchial cysts. This is consistent with previous studies except in cases for dermoid cysts where no sex difference has been noted, but it can be attributed to poor female health education in our set up. The sex ratio in remaining cysts can not be commented upon due to less number of cases.

The average age of patients at the time of presentation was 36.1 years in case of sebaceous cysts 33.8 years in thyroglossal cysts and 33.1 years in branchial cyst. Patients with dermoid cysts presented between 2nd and 3rd decade of life concurs with previous reports, (sebaceous 38-3 years, thyroglossal 32 years, dermoid 2-3rd decade and branchial 34 years)[1,3,6,7].

Majority of the dermoid cysts (56.8%) involved neck followed by floor of mouth (26.6%) and bridge of nose (16.6%). 13 (72.2%) case of thyroglossal cysts were situated in infrahyoid, 5 (27.8%) in suprahyoid region. In all the cases tract was seen running anterior to hyoid bone. Out of the 12 branchial cysts 9 (75 per cent) were seen in the upper half of the neck at the junction of upper 1/3rd and lower 2/3rd of sternomastoid muscle along its anterior border and 3 (25%) in the lower half of the neck. At surgery one case was found to have extension of the cyst between the carotid vessels towards pharynx. Most cases of sebaceous cysts were found in the region of face and forehead followed by auricular region (29.4%) and neck (26.4%).

Our observation regardings the site of involvement of above mentioned cysts are in quite confirmity with previous studies except for sebaceous cysts (auricular region 1-3%, neck 2.5% face and forehead 31.9%).[1,2] This is because the reported incidence in previous studies involved whole body.

Majority of patients in this study presented with swelling (92.7%) followed by pain, fever and dnasal obstruction (5.4%). The two patients with vocal cord cysts complained of hoarseness of voice while stridor was the chief complaint in patients with vallecular cysts. Aspiration cytology was carried out in all clinically accessible cysts. The cytological diagnosis made in 99 cases was confirmed by histological examination. The results of aspiration cytology were in confirmity with the results of histological examination in all the (99) cases. Our observation is well supported by previous studies where cytological diagnostic accuracy is reported as (100%)[4,8] Except in two cases of dental cysts were patches of squamous metaplasia were seen, the remaining cysts of the present study exhibited a normal epithelial pattern.

Excisional biopsy was employed as the standard method of treatment for all the cases except in two cases of vallecular cysts, where marsupilisation was done. The incidewnce of wound infection following surgery was slightly higher as compared to the previous studies and we attribute this to poor patient compliance while as high percentage of recurrence and haematoma formation is explained by less number of patients in the present study as compared to previous studies.

Conclusion:

Sebaceous, dermoid, thyroglossal and branchial cysts are th commonest types of the cysts encountered in otolaryngological practice. The time interval between the appearance of the lesion and presentation to a clinician varies from less than 6 months to 2 years or more. Aspiration cytology is confirmatory for diagnosis in all cystic lesions if performed correctly, total excision of the cyst must be performed to avoid recurrence. Vallecular cysts are best managed by marsupilisation. On the whole post operative complications like haematoma, infection and recurrence are infrequently encountered.

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Comparative Evaluation of Endoscopic and conventional surgical techniques in the management of Nasal polyposis

V.P.Venkatachalam MS; Arun Bhat MS.

Abstract: *Fifty patients who were diagnosed to be suffering from nasal polyposis constituted the study. They were randomly divided into two groups A&B of 25 patients each. Patients belonging to Group-A (Study) were treated by Functional Endoscopic Sinus Surgery and the patients belonging to Group-B were treated by conventional techniques i.e. Simple polypectomy with or without Caldwel-Luc's operation, intranasal ethmoidectommy, Frontoethmoidectomy, sphenoethmoidectomy etc. The follow-up period varied from 6-30 months. In the study group, out of 25 patients, 18 patients (72%) had complete relief of symptoms, 4 patients (16%) had partial relief and 2 patients (8%) had no relief of symptoms. In the control group, 12 patients (48%) had complete relief, 9 patients (36%) had partial relief and 3 patients (12%) had no relief of symptoms. The results of the series reveal that the endoscopic sinus surgery is an important tool in the armamentarium of rhinologist in dealing with nasal polyposis due to its precise and atraumatic removal of aetiological factors.*

Key words: *Nasal Polyposis, Functional Endoscopic Sinus Surgery, Conventional Technique*

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Introduction

Nasal polyposis accounts for the most commonly encountered pathological manifestation of the mucous membrane lining the nose and paranasal sinuses. After chronic sinusitis, nasal polyposis is the next commonest indication for surgical intervention in this area.

Nasal polyposis is an extreme form of chronic infection of the paranasal sinuses and has been known for thousands of years.[1] But it is surprising to note that there is no information about the prevalence of adult nasal polyposis even in recent textbooks on rhinology. In India, no statistics are available about the prevalence rate of nasal polyposis. Van Disboek[2] estimates that approximately 5% of the population is affected by this condition. In Europe about 1-2% of the adult population are affected by nasal polyposis[3].

Management of a patient with nasal polyposis is frustrating to both the patient as well as treating clinician due to its high rate of recurrence and therefore it poses a significant challenge to a rhinologist. Although the pathophysiology of nasal polyp is still uncertain, yet a number of factors like infectioon, allergy, trauma, pollutants, metabolic diseases and psychogenic factors have all been implicated either singly or in combination in its aetiopathogenesis.

The surgical management of nasal polyps have undergone many modification since the time before Hippocrates (463-370 BC) when 'Sponge method' was employed for remove polyps[1]. In spite of a variety of surgical options available, till recently medical therapy remained the mainstay of all the treatment regimens.

Conventional surgical methods for treatment of nasal polyps include intranasal polypectomy alone or in combination with Caldwel-Luc's operation. Harris Mosher (1912) described a method of intranasal extirpation of ethmoidal labyrinth.[4] Other operations performed for multisinus diseases include Jansen-Horgan operation, Lynch Operation and Ferris-Smith external ethmoidectomy.

Silverstein and McDaniel (1987)[5] used microscope to perform sphenoethmoidectomy for polyp. However, it was found that the microscope does not allow visualisation of the nooks and corners of the nasal cavity. Also a high incidence of complication were reported in all these techniques.

The work by Messerklinger[6] on endoscopy of the nose and paranasal sinuses revealed that the key factor in the initiation and perpetuation of the sinus diseases in the 'ostiomeatal complex' and based on this concept described a surgical technique to treat sinus diseases. Later on this technique was propagated by his student Stammberger[7] in Europe and by Kennedy[5] in United States.

Larson and Tos[9] observed that majority of the polyps occurs in the mucosa of the middle meatus and since the pedicles are frequently located in the anterior ethmoids,

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this makes the disorder amenable and accessible to a circumscribed anterior ethmoid surgical procedure such as functional endoscopic sinus surgery.

Since very few studies have been reported wherein the results of functional endoscopic sinus surgery has been compared with conventional surgery, we undertook the present study to evaluate the effects of Functional Endoscopic Sinus Surgery (FESS) viz-a-viz Conventional Surgery (CS) in terms of results and complications in the treatment of nasal polyposis.

Material and Methods

Fifty patients presenting with nasal polyposis attending the out-patient department of ENT, Safdarjung Hospital, New Delhi during the period from June 1993 - December, 1995 constituted this study. After taking a detailed clinical history, all the patients were subjected to a meticulous Ear, Nose and Throat examination followed by a thorough physical examination. Before subjecting the patients to surgery, they were put through a standard protocol of investigations which included, routine haematological examination, urine examination and plain radiological evaluation of Nose and Paranasal sinuses (Occipitomental, Occipitofrontal and Lateral view).

Once a diagnosis of nasal polyposis was confirmed on the basis of history, clinical and radiological examinations, the patients were divided into two groups of 25 patients each. Group-A (study) patients, who were to be treated by Functional Endoscopic Sinus Surgery (FESS), were subjected to a diagnostic nasal endoscoopic examination under local anaesthesia to assess the extent of the disease as well as to stage the polyps as per Levine's classification.[10]

Stage - I	:	Confined to middle meatus.
Stage - II	:	Anterior to middle turbinates extending inferiorly to inferior tubinate.
Stage - III	:	In addition to being anterior to middle turbinate extending meadialy and posteriorly.
Stage - IV	:	Extending to the floor of the nose with parts of turbinates visible.
Stage - V	:	Filling the nasal cavity completely obscuring the turbinates.

Computerized Tomography (CT) of the nose and paranasal sinuses (screening Axial and Coronal if needed without contrast) was done in patients where the extent of the disease could not assessed by clinical and diagnostic endoscopic examination.

All the operations in Group-A patients were performed under local anaesthesia employing the classical Messerklinger Technique Functional Endoscopic Sinus Surgery (MT-FESS).[6,7] Group-B patients were operated under either local or general anaesthesia and the technique employed depended on the extent of the disease. The complications enountered in the two groups were noted. A meticulous follow-up was carried out initially on alternate days for a week, then biweekly for 2 weeks and thereafter at 2 weekly interval. All the patients were postoperatively put on steroid nasal spray (Budesonide) 2 Puffs twice a day for 6 months.

The response to treatment was graded as under:

Complete	:	90-100% relief
Good	:	75% - 90% relief
Fair	:	50% - 75% relief
Poor/no response	:	<50% relief

Observation

50 diagnosed cases of nasal polyps constituted the study. They were divided into two groups of 25 case each. Majority of the patients were in the age group of 20-39 years with the males outnumbering the females by 2.3:1. Nasal obstruction was complained of by all the patients. The complaints included nasal discharge in 27 patients (54%), Headache in 10 patients (20%), nasal bleeding in 10 patients (20%) and excessive sneezing in 8 cases (16%). The duration of symptoms varied from 6 months -36 months. All the patients who presented to us had taken some form of medication without any satisfactory relief of symptoms and fourteen patients gave history of having undergone some surgical procedure without any benefit. Table-I depicts the anterior rhinoscopic findings in all the 50 patients. Table-II (a) and Table II (b) reveals the X-ray PNS findings in the two groups of patients. Diagnostic nasal endoscopy was performed in all the patients who were to be subjected to functional endoscopic sinus surgery and the detailed findings are shown in Table-III. CT scan was performed in 21 patients where the actual extent of the polyp could not be assessed by diagnostic nasal endoscopy and it revealed involvement of anterior ethmoid cells in all the cases. The other findings seen are depicted in Table-IV. In the study group 39 procedures were carried out whereas in the control group 36 procedures were carried out. The details of the various procedures carried out in the two groups are shown in Table-V (a) and V(b). The various complication seen in the two groups are depicted in Table-VI. The follow-up period varied from 6-30 months with a mean follow up of 16.5 months.

In the study group, out of 25 patients, 18 patients

(72%) showed complete relief of symptom, 3 (12%) good response and 1 (4%) showed fair response and 2 (8%) patients had no relief of symptoms and one patient was lost of follow-up.

In the control group, out of 25 patients, 12 patients showed complete response, 6 (24%) had good response and 3 (12%) had fair response to treatment. 3 (12%) had no relief of symptoms and 1 (4%) patient was lost to follow-up.

Discussion

Management of Nasal polyposis is a tricky problem to a treating clinician due to multiplicity of aetiological factors. The technical advancement made in the Hopkin's rod system of endoscopes coupled with the work by Messerklinger on the nasal and paranasal sinus mucous and mucociliary transport have greatly revolutionised the management of nasal polyps.

It has been thought for a long time that the cause for persistent infection in the paranasal sinus is nasal obstruction. However, the work by Messerklinger and later on by Stammberger have shown that a diseased ostiomeatal complex plays an important role in the pathogenesis and perpetuation of the chronic disease of the sinus. The disease starts in the narrow clefts of the lateral wall of the nose mainly the anterior ethmoidal air cells. The ostia of the larger sinuses which drain into middle meatus, get blocked if there is disease in the anterior ethmoidal cells. This in turn leads to a vicious cycle of stasis, infection anhd further oedema. These cause seemingly by irreversible changes in the larger sinuses. Also the anterior end of the middle turbinate is more prone to oedema and hypertrophy since it bears the brunt of the atmospheric pollutants, allergens etc. Other factors that influence the susceptability of anterior ethmoidal complex to infection include anatomical variation like paradoxical middle turbinate, medially or laterally bent uncinate process, pneumatized uncinate process, concha bullosa and a large buila ethmoidalis.

The infection of the sinuses in turn leads to nasal polyp formation. Besides infection, allergic element also play a part in polyp formation in a certain percentage of individuals. Functional endoscopic sinus surgery aims to clear the disease in the anterior ethmoidal complex and re-establish ventilation and drainage of the larger sinus so that the disease process gets reversed in the larger sinus without even touching the sinus mucosa.

In the present study consisting of 50 patients of nasal polyposis, the majority of the patients were in the age group of 20-29 with the males outnumbering the females by a ratio of 2.33:1. These findings are similar to the findings of Rice (1989).[9]

The high incidence of polyps in the third and fourth decades of life probably explains the possibilities of infection and vasomotor imbalance (Drake Lee, 1987) as an aetiological factor in the polyp formation, since this age group is vulnerable to infection, anxiety and conflicts and tension of day to day life. Also patients of this age group are exposed to a variety of pollutants daily, due to their increased activity which in turn leads to allergic reaction of the nasal and paranasal mucosa, thus predisposing them to polyp formation.

Commonest presenting symptom was nasal obstruction and discharge which is similar to the findings of Levine (1990)[10] and Frenkiel et al (1982).[12]

Plain X-ray of the paranasal sinus was not of much utility. Diagnostic nasal endoscopy was performed in all the patient in the study group to assess the extent of the disease as well as to note down the various factors responsible for obstructed osteomeatal complex like medially rotated or pneumatised uncinate process, paradoxical middle turbinate and deviated nasal septum. Staging of the polyps was done as per Levine's staging system[10] to assess the extent of the disease and also its response to the treatment. In this study the success or failure of the treatment was same irrespective of the various stages of polyps.

Computerized tomography was done in those cases where the exact extent of the polyp couldn't be assessed by other means namely clinical examination, plain x-ray of the paranasal sinuses and nasal endoscopic examination. It revealed the involvement of anterior ethmoidal complex in all the cases thereby suggesting that the disease process first originates here and later on spreads to other areas.

In the study group 39 procedures were carried out. Although polyp was seen only in 38 nasal cavity of this group yet on endoscopic sinus surgery polyp/polypoid mucosa was present in 9 more cases. It was present mainly in infundibulum bulla ethmoidalis and anterior ethmoidal cells. Levine (1990)[10] showed polyps in 39 out of 119 patients suffering from chronic sinusitis at the time of operation.

In the study group out of 25 patients 18 patients (72%) showed complete response whereas 4 patients (16%) showed fair response which is consistent with the findings of Levine (1990).[10]

In the control group (conventional surgery), out of 25 patients 12 patients (45%) showed complete response and 9 patients (36%) howed fair to good response. Lawson (1994)[13] reported a complete success rate of 73% in 90 patients who underwent traditional surgery. Sogg (1989) reported complete relief of symptoms in 51% of cases who underwent conventional surgery. The discrepancy in these series as also ours may be due to the different reporting system, presence of allergic element and extent of the disease.

The present study has revealed that in the management of nasal polyps the results with functional endoscopic sinus surgery is better than conventional surgery both from the relief of symptoms as well as decrease incomplications. Functional endoscopic sinus surgery is a safe, efficient modality for dealing with nasal polyposis. It can be carried out under local anaesthesia. Due to the deflected angles of telescopes it is possible to precisely remove the disease from nooks and corners of the nasal cavity. Because of the precise surgery, bleeding is minimal and no packing is required. Hospital stay of the patient is reduced and hence it is economical. However Functional endoscopic sinus surgery is not suitable for polyposis due to extensive fungal infection, extensive polypoid inverted papilloma and rhinosporroidosis. Also, it is not suitable if there is associated intracranial extension or erosion of the bony walls of the sinus. Any associated allergy has to be dealt with separately on its merit.

In the light of our above observations, we feel that functional endoscopic sinus surgery is an important tool in the armamentarium of a rhinologist dealing with nasal polyposis.

Table-I
Anterior Rhinoscopic Findings (n=50)

Nasal discharge	50
Polyp	50
Inferior Turbinate hypertrophy	21
Middle turbinate hypertrphy	18
Deviated Nasal septum	9

Table-II(A)
Radiological findings (X-ray PNS)
(Study group; n=25)

	Frontal		Maxillary		Ethmoidf	
	Uni	Bil	Uni	Bil	Uni	Bil
Hazziness	1	2	9	6	-	-
Fluid level	-	-	1 1	-	-	-
Polyp	-	-	12	-	-	-
Thickened Mucosa	-	-	9	1	-	-
Hypoplasia	-	2	-	-	-	-

Table-II(B)
Radiological findings (X-ray PNS)
(Control group; n=25)

	Frontal		Maxillary		Ethmoid	
	Uni	Bil	Uni	Bil	Uni	Bil
Hazziness	3	3	9	3	7	9
Fluid level	-	-	1	-	-	-
Polyp	-	-	6	3	-	-
Thickened Mucosa	-	-	4	9	-	-
Hypoplasia	2	-	1	-	-	-

Table -III
Diagnostic Nasal Endoscopy findings
(n=25)

Polyps	25
Mucopus/pus	25
DNS	5
Concha Bullosa	2
Paradoxical Middle Turbinate	9
Medially rotated uncinate process	6

Table -IV
CT Scan Findings
(n=21)

Hazziness

Ant. Ethmoid	21
Post Ethmoid	15
Maxillary	18
Sphenoid	3
Frontal	3
Concha Bullosa	3
Deviated Nasal Septum	5

Table-V(a)
Surgical Procedures Performed in Study Group
(n=39)

Anterior EWthmoidectomy + Middle Meatal Antrostomy (MMA) + Polypectomy	12
Polypectomy + MMA+ Uncinectomy	15
Polypectomy + Total ethmoidectomy + MMA	9
Polypectomy + Total Ethmoidectomy + Sphenoidotomy	3

Table-V(b)
Surgical procedures in the Contrl Group
(n=36)

	Unilateral	Bilateral
Paranasal Polypectomy	10	6.
paranasal po9lypectomy + Caldwell-Luc	5	-
Intranasal polypectomy + Ethmoidectomy	3	2
External Ethmoidectomy + Partial Maxillectomy + Polypectomy	2	-

Table -VI
Complications (n=50)

	Group-A (Study) (n=25)	Group-B (Control) (n=25)
Bleeding	3	2
Synechia	5	13
Wound infection	4	7
Orbital Haematoma	-	2
CSF Rhinorhoea	-	0
Loss of vision	-	-
Lamina Papyracea (damage)	1	2

Table-VII
Results (n=50)

	Group-A (Study) (n=25)	Group-B (Control) (n=25)
Complete relief	18(72%)	12(48%)
Good relief	3(12%)	6(24%)
Fair relief	1(4%)	3(12%)
No relief	2(8%)	3(12%)
Lost to follow-up	1(4%)	1(4%)

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Role of Buprenorphine Hydrochloride in Attenuating the Haemodyanamic, Hormonal and Metabolic Responses to Surgery in Children

Abdul Qayoom Lone MD.; Imtiyaz Naqash MD.; Shigufta Qazi MD.; Khurshid Alam Wani MS.

Abstract: *Fifty healthy children, in the age group of 5 to 12 years, undergoing elective short surgical procedures were randomly allocated to two groups of 25 patients each. Group I (control group) received no analgesia during the study period, while in group II (study group), patients received buprenorphine hydrochloride in the dose of 5 ug per kg body weight intravenously, 5 minutes before induction of anaesthesia. Rest of the anaesthesia technique was common to both the groups. The parameters studied included the heart rate, blood pressure, serum cortisol, serum prolactin and blood sugar estimations, which was done just before induction of anaesthesia, during endotracheal intubation, at the time of skin incision and during recovery from anaesthesia. Heart rate, blood pressure and serum prolactin level showed a significant ($P< 0.01$) elevation in both the groups but the percentage elevation was more in control group. Serum cortisol level showed significant elevation in control group only. Blood sugar was elevated significantly at incision and recovery phases in control group and during recovery in study group.*

Key words: Stress response; Endocrine response; Metabolic response Surgery; Paediatric; Narcotic; Buprenorphine hydrochloride.

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Introduction:

Noxious surgical stimulation is accompanied by profound changes in endocrine function that are generally referred to as the stress responses to operation and trauma. It activates two major pathways in the body, the pituatary adreno-cortical system and sympathetic adreno-medullary system.[1]

The general pattern of the endocrine responses to operation includes, a pitutary of trophic hormones from the hypothalamus which stimulate the pitutary release of ACTH, growth hormone, prolactin, endorphine and ADH, increased secretion of catabolically acting hormones (cortisol, catecholamines, glucagon and thyroxine) and decreased or unchanged release of anabolically acting hormones such as insulin and testosterone.

The release of stress hormones stimulates a cascade of metabolic changes leading to substrate mobilisation with the breakdown of protein, fat and carbohydrate stores.[2] These responses particularly following major surgery may lead to pathological degree of metabolic instability with increased morbidity and mortality.

In general, release of catabolic stress hormones during and after operation precipitate metabolic adjustments. Within physiological limits these endocrine metabolic changes may facilitate wound healing and recovery, but if severe or prolonged, these may precipitate post operative complications leading to an increased morbidity and mortality. Paediatric stress responses are relatively greater in magnitude and young children in particular are susceptible to the deterimental effects of a severe stress response because of their inherent metabolic characteristics. Remarkably little is known about the hormonal and metabolic responses of infants and young children and specific analgesia regimens for this purpose need to be evaluated. In recent years considerable interest has been shown in the ability of opoid analgesics to modify the endocrine and metabolic responses to surgery.

The present study was undertaken to find out the role of synthetic narcotic, buprenorphine hydrochloride, in modifying the haemodyanamic, hormonal and metabolic responses to surgery in children.

Methods:

Fifty children of either sex, ASA I, aged between 5 and 12 years undergoing elective short surgical procedures were taken up for the study. Written and informed consent to participate in the study was taken from the parents. No premedication was given to any of the patietns. For the purpose of study, patients were randomly allocated to two groups of 25 patients each. Group I (Control group) patients did not receive any

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analgesia during the study period. Group II (Study group) patients received buprenorphine hydrochloride 5 ug per kg body weight 5 minutes before induction of anaesthesia.

The general anaesthesia technique was similar in both the groups. No inhalational agent was used in either of the groups. During the study period all patients received normal saline 5 ml per kg per hour through intravenous line. Heart rate and blood pressure were constantly monitored and recorded at 10 minutes intervals during the procedure. Blood samples for estimation of blood glucose, serum cortisol and serum prolactin were drawn from the opposite arm at following occasions"

1. Pre-induction: before induction of anaesthesia, but 5 minutes after administration of buprenorphine hydrochloride in group II patients.
2. Endotracheal intubation (ETI)
3. Skin incision (INC)
4. During recovery (REC)

Blood glucose estimation was done by glucose oxidase method, while as serum cortisol and prolactin levels were estimated by radio immune assay techniques. Statistical evaluation was done by students 'T' test where P<0.001 was taken as highly significant.

Results:

The estimation of pre-induction levels of each parameter was considered as the basal control level for that patient and the subsequent findings were compared with the same. The age and weight of the patients in both the groups was comparable (Table-I). There was a highly significant elevation in heart rate and systolic and diastolic blood pressures (P<0.001) at all stages in both the groups compared to pre induction values. However the percentage elevation was more in group I as compared to group II (Tables II & III). Table IV shows changes in serum cortisol, serum prolactin and blood sugar at different stages. The serum cortisol showed a highly significant rise in group I patients at different stages compared to pre induction level, where as the rise in serum cortisol in group II patients was insignificant during different occasions. Serum prolactin estimation showed a significant rise at endotracheal intubation and highly significant rise at skin incision and during recovery in both the groups. There was significant rise in blood sugar at skin incision in group I patients only, where as rise in blood sugar was highly significant in both the groups during recovery when compared to pre inductiuon levels.

Discussion:

Recently considerable interest has developed in the anaesthetic techniques which ameliorate some of the physiological and metabolic responses to surgery, so called stress free anaesthesia. Among the advantages that these techniques may confer are cardiovascular stability[3], a reduction in the endocrine and metabloic responses to surgery[4], and an improvement in post operative nitrogen balance.[5] At present two main methods are available to suppress the hormonal and metabolic responses to surgery. These include local analgesic techniques such as epidural and spinal analgesia to modify the stress responses.[6] Secondly supplementation of anaesthesia with large doses of analgesics such as morphine and fentanyl which have been shown to reduce or even abolish hormonal and metabolic changes during surgery.[7]

Buprenorphine hydrochloride is a synthetic narcotic, highly potent, long acting and exhibits powerful agonist activity. Following systemic administration peak concentrations are achieved within 5 minutes and analgesia lasts for 6-8 hours.[8]

The results of our study showed significant to highly significant variation in heart rate and blood pressure in both the groups compared to preinduction values but the percentage elevation was seen to be more in control group where no analgesia was used. Serum cortisol and blood sugar levels were increased in control group. The mechanism responsible for changes in serum cortisol are activation of neuroendocrine and sympathoadrenal systems and as a consequences of the ACTH release, increased adrenocortical secretion. In group II patients, the rise in cortisol level was found to be modified by the administration of buprenorphine hydrochloride as analgesia. Our results are in accordance with Hall et al,[9] who also found rise in serum cortisol level being abolished in patients receiving fentanyl as analgesia. Serum prolactin levels increased significantly in both the groups but percentage elevation was found to be more in the control group.

From these observations it can be concluded that administration of buprenorphine hydrochloride in paediatric patients undergoing surgery attenuates the stress response reflected by haemodynamic, hormonal and metabolic hydrochloride is recommended to avoid haemodynamic and biochemical derangements during surgery particularly in patients where such disturbances are least desired.

Table - I: Mean age and weight of patients in two groups

Groups	No of cases	Age (years) Mean + SD	Weight (kgs) Mean + SD
I	25	7.90 +2.25	20.60 +6.50
II	25	9.22 +2.45	25.06 +7.94

Table-II: Comparative changes in heart rate at different stages between the two groups.

Stage	Heart Rate(beats/minute) Group I Mean+ SD	% Elevation	Group II Mean+ SD	% Elevation
Pre-induction	100.76 + 7.99		96.20 + 8.08	
Endotracheal intubation	132.48**+8.25	31.48%	108.92**+9.63	13.22%
Skin incision	132.64**+7.26	31.64%	109.16**+10.44	13.47%
Recovery	140.08**+ 8.12	39.02%	115.56**+8.85	20.12%

**Highly significant (P<0.001)

Table - III: Comparative changes in blood pressure at different stages between the two groups.

Stage	Blood Pressure (mm Hg) Group I Systolic Mean + SD	Diastolic Mean + SD	Group II Systolic Mean + SD	Diastolic Mean + SD
Pre-induction	102.4+8.50	68.72+5.24	105.80+8.84	68.52 + 8.88
Endotracheal intubation	128.52+8.20**	77.84+11.02**	115.30+7.22**	80.52+8.41**
Skin incision	127.28+8.12**	73.08+8.84**	114.52+7.80**	80.40+7.58
Recovery	134.58+7.18*	80.88+8.22**	121.24+8.02**	74.84 + 8.77**

* Significant (P < 0.01)
** Highly significant (P <0.001)

Table - IV: Changes in serum cortisol, serum prolactin and blood sugar levels in the two groups.

Stage	S. Cortisol (ug/dl) Group I Mean + SD	Group II Mean +SD	S. Prolactin (mIU/l) Group I Mean +SD	Group II Mean +SD	Blood Sugar (mg%) Group I Mean +SD	Group II Mean +SD
Pre induction	16.25 +7.22	16.32 +7.73	415.75 275.93	549.05 +395.70	76.24 +13.10	74.96 +9.99
ETI	20.65* +7.27	16.42 +6.69	605.56* +385.78	780.49* +378.60	81.20 +9.87	83.32 +14.58
INC	22.61* +8.51	18.63 +10.27	996.76** +525.52	1237.60** +450.74	83.68* +8.92	79.76 +11.16
Recovery	27.00** +9.51	21.11 +9.52	1310.69** +532.88	1328.97** +581.73	92.96** +12.01	92.76** 18.17

* Significant (P < 0.05)
** Highly significant (P< 0.001)

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Wilson's Disease-A Case Report and Review of Literature

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***Abstract:** We describe an 11 year old boy with signs and symptoms of cirrhosis of liver. He had a low ceruloplasmin level with elevated urinary copper excretion. The diagnosis of Wilson's disease was confirmed with liver biopsy which demonstrated mixed macro-and micronodular cirrhosis with copper deposition in hepatocytes and phagocytes. He was started on pencillamine therapy with excellent response. Over a period of 20 year follow-up he has manifested psychiatric disturbances, primarily during the time he was non-complaint with therapy. Currently he is back on pencillamine treatment and is doing well.*

***Key words:** Wilson's Disease; Copper; Ceruloplasmin; Cirrhosis;*

JK - Practitioner 1998; 5(4): 303 - 305

Introduction:

Wilson's disease is an inherited disorder of copper metabolism characterized by accumulation of excessive copper first in the liver and later, when binding sites there are saturated in the brain, cornea, kidneys and red blood cells. The clinician should consider this diagnosis when evaluating neurologic or behaviour distrubances and concurrent hepatic dysfunction. However, wide spectrum of clinical presentation of Wilson's disease can mislead a clinician and result in irreversible damage to the brain and liver. We describe a young boy who demonstrated several features of Wilson's disease and it's favourable response to treatment. His 20 year follo-up typifies the natural history of the disease.

Case Report:

An 11 year old boy of German descent was admitted with two week history of progressive abdominal swelling. He was anorectic, however, denied any history of sore-throat, fever, rigors, chills, oliguria or any other symptom. His development milestones were normal for his age.

On physical examination he was afebrile with normal vital signs. His height and weight was appropriate for his age. No icterus or pallor was noted. The abdominal examination revealed visible overlying veins, hepatosplenomegaly and ascites. He also had bilateral pedal edema. The chest, cardiovascular and neurologic examination were normal. He did not demonstrate any other signs of chronic liver disease. A complete eye examination, including slit-lamp examination was also normal.

The laboratory data including complete blood count, renal profile and urine analysis was normal. The serum albumin was 2gm% and 24 hour urinary protein was 300mg/L. The total serum cholesterol was 143mg/dl. The liver function tests showed total bilirubin of 2.3mg% (Normal: 0.5-1.0mg%), AST of 87 IU/L (Normal: 13-45IU/L), ALT of 54 IU/L (normal: 13-44 IU/L) and alkaline phosphatase of 100 IU/L (Normal: 80-110). The prothrombin time was 15.2sec (Normal: 12-14sec). the abdominal ultrasound showed ascites, splenomegaly with normal liver architecture and no masses. The hepatitis screening for Hepatitis A, B and C was negative. The ascitic fluid proved to be a transudate. Serum alphafetoprotein level was normal. The collagen vascular screening serology was negative and complement levels were normal. The serum ceruloplasmin level was 12mg/dl (Normal: 20-50mg/dl) and serum copper level was 172 micrograms/dl (normal: 70-155 micrograms/dl). The 24 hour urinary copper level was 765 micro grams/d (Normal 15-50 micro grams/d)The diagnosis of Wilson's disease was confirmed with an open liver biopsy which showed firm, pale and multinodular liver. The histopathology of liver specimen showed mixed macro and micronodular cirrhosis, proliferation of bile-ducts, collapse of some hepatocytes and random lymphocytic infiltrate. The rhodanine stain demonstrated copper in hepatocytes and phagocytes.

The patient was started on pencillamine and Zinc therapy with favourable response. He was followed as an outpatient with monitoring of his urinary copper and Zinc levels for about three years when he was lost to follow-up. Four years later he was admitted to the psychiatric floor following a suicidal attempt. At this time he was found to be non-complaint with treatment. The therapy was reinstituted and patient started to feel better again and is currently being followed on outpatient

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these years did not reveal Kayser-Fleischer's ring nor did he develop any neurologic dysfunction.

Discussion:

Wilson's disease was first described in 1912 by Kinnear Wilson as a familial disease characterized by progressive, lethal neurologic disease with chronic liver disease and Kayser-Fleischer's ring.[1] It is a disease of copper accumulation with autosomal recessive pattern. The gene is located on the long arm of chromosome 13 near the esterase D locus.[2] The mutation, usually spontaneous involving the gene disrupts the function of P- type ATP ase required for copper transport and excretion by the liver.[3] Although the biochemical defect is present at birth, clinical symptoms typically appear for the first time in the older children, adolescents and young adults. The extent of the genetic defect has been correlated with the clinical severity, in that larger defects appear to result in the development of symptoms at a younger age.[4]

Most patients present with hepatic or neurologic dysfunction or both, although psychiatric, ophthalmological, hematologic, renal, musculoskeletal, cardiac, endocrinological and dermatological presentations have all been described. Upto 30% patients with Wilson's disease present with clinical, biochemical and histologic features similar to those of other forms of chronic hepatitis. Therefore biochemical screening should be performed in all patients under the age of 40 years in whom the clinical or histologic findings are consistent with chronic hepatitis and autoimmune and viral disorders have been excluded.[5] The hepatic damage ranges from mild steatohepatitis to fulminant hepatic failure. The later shows 72% survival rate with liver transplantation at 5 years and complete reversal of underlying defects in copper metabolism.[6] The other clinical manifestations commonly include neurologic dysfunction in the form of tremor, dystonia, dysarthia, choreoathetosis and ataxia. Psychiatric features include depression, homicide, suicide, cognitive impairment and rarely dementia. The Kayser-Fleischer's ring may be formed due to copper deposition in the decemet's membrane of cornea and appear as a golden, brown or green ring under the slit-lamp examination. Rarely Wilson's disease has been associated with rhabdomyolysis,[7] autoimmune hemolysis,[8] secondary ammenorrhea and abortions.

The patient with the classic combination of chronic liver disease, tremor or dystonia and Kayser-Fleischer's ring is readily diagnosed on clinical basis to have Wilson's disease but patients such affected are uncommon. The suggestive clinical features should lead to further work-up, including a careful slit-lamp examination of the eyes for KF ring. The KF ring is very helpful in diagnosis especially with low ceruloplasmin levels, however, it commonly appears in conjunction with neuropsychiatric disturbances and may be absent when only hepatic involvement is present, as in our patient. Serum ceruloplasmin level is typically low, however a normal concentration may be found in at least 5% of patients. The serum copper concentration is low. The non-ceruloplasmin bound copper concentration is elevated. the studies of urinary copper excretion prove useful for diagnosis and reveal increased daily urinary copper excretion. The hepatic tissue copper levels are usually greater than 250 micrograms/gram of dry tissue weight and are considered diagnostic of Wilson's disease. The negative copper stains in liver specimens, however, do not exclude the diagnosis as deposition may be heterogenous. The other histologic features in the liver include glycogen deposits, Mallory bodies, fibrosis and submassive necrosis. All patients with Wilson's disease, symptomatic or asymptomatic require treatment. Therapy is usually directed towards bringing copper levels back to normal, which is accomplished by copper-free diet and chelation. Pencillamine is mostly used as a first line to chelate copper at dose of 1-2g/day but unfortunately neurologic symptoms may worsen in 25% of patients. Another coppr chelator, trianterene has produced some successful results but colitis is a potential adverse effect in long term therapy. Recently FDA approved Zinc-acetate (Galzin) for the treatment of Wilson's disease which acts by blocking the absorption of copper in the intestinal tract and is generally well tolerated. Tetrathiomolybidate is used as an initial therapy in many institutions, especially in patients who develop neurologic deterioration with pencillamine. This drug forms a tripartite complex with copper and protein, blocks copper absorption from the intestines and may render copper less toxic. The screening of asymptomatic siblings of patients with Wilson's disease can be done by 24-hour urine measurement of copper and DNA linkage analysis with Polymerase chain reaction. For asymptomatic relatives a urine test should be done at age 5 years and again at age 15 years. Screening for low ceruloplasmin for abnormal liver function tests can begin at age 2 years.[9]

Our patient presented in the typical age group for Wilson's disease with predominant hepatic manifestations that resolved with pencillamine therapy. He later developed psychiatric disturbances which also resolved completely with treatment. Screening of his relatives revealed only one sibling with elevated serum levels, though with normal ceruloplasmin. She was also basis. The repeated ophthalmologic examinations over treated with pencillamine and Zinc.

In summary, clinicians should consider Wilson's disease in young patients with unexplained hepatic, ocular or neuropsychiatric disturbances. Effective treatment is available which can prevent irreparable damage to various organs. With appropriate screening methods asymptomatic patients can be detected even before any organ damage becomes obvious.

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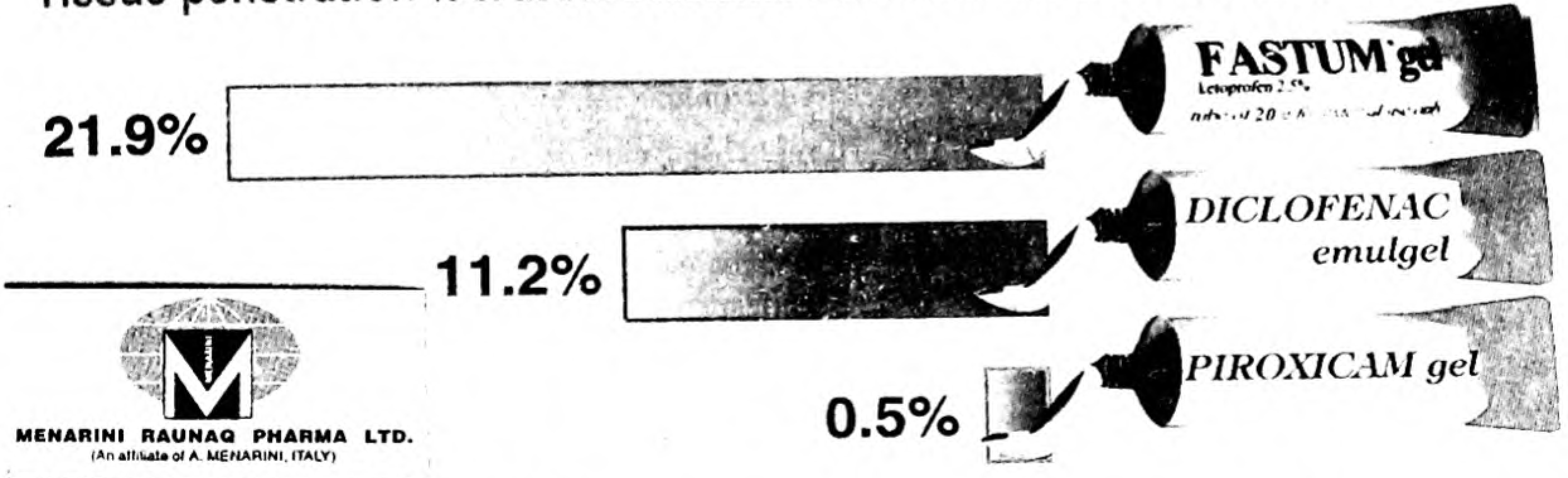

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"Extragonadal Germ Cell Tumor with Atypical Presentation

Abdul Ahad MS,; Zahoor Ahmad MS.

Abstract: *Extragonadal germ cell tumor is a rare malignancy, mediastium being the commonest site. Its occurance in neck is rarely encountered in clinical practice. Here we report a case with this atypical presentation.*

Key words: *Germ cell tumor, Atypical presentation, Rare-malignancy, Surgical debulking.*

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Case Reports

A 56 year old female presented with a gradually enlarging midline neck swelling extending from suprasternal notch to upper border of thyroid cartilage. Examination revealed firm, nontender, ulcerated, nodular midline swelling with dimensions of 15 cm x 15cm fixed to underlying structures. Rest of ENT examination was normal. Hematocrit was normal. FNAC was suggestive of germinoma. Beta HCG titre was 1652 m/u. An incisional biopsy specimen was diagnostic of a germ cell tumor showing two distinct cell types; one is large well defined spheroid cells with spherical nuclei, other type is small darkly stained cells interespersed among spheroid cells, typical of a germinoma. Primary surgical debulking was done and the patient was given post operative radiotherapy with adjuvant chemotherapy. She received five courses of cisplatin, bleomycin and vinblastin 5mg/m^2 and is recurrence free after 3 years.

Discussion:

Germ cell cancer is a rare malignancy accounting for 1% of all cancers. Extragonadal germ cell tumors represent less than 2% of all germ cell tumors. These tumors have been commonly found in mediastinum and retroperitoneum and less commonly in intracranial, submental and presacral regions. Primary surgical debulking followed by radiotherapy and adjuvant chemotherapy has resulted in excellent response in this case as the patient is recurrence free after 3 years of follow up. Several authors have stressed the importance of surgical debulking in patients with extragonadal germ cell malignancies.[4,5,6,7] Our experience supports this observation. Some authors have seen shorter duration of response by using chemotherapy alone in extragonadal germ cell tumors.[3,4] Combination chemotherapy based primarily on cisplatin, vinblastin and bleomycin followed by surgical debulking of residual tumor in partial responders has increased the number of long term survivors.[1,2] Our experience substantiates the view that primary surgical debuling gives more favourable outcome in extragonadal germ cell tumors as compared to surgical debulking after chemotherapy. This has been supported by previous workers. Treatment of germinomas of gonadal and extragonadal origin by adjuvant chemotherapy following surgery and/or radiotherapy constitutes one of the real successes of cancer therapy. Because of the excellent response to this treatment regime with a cure rate of upto 80%, human GCT is an important model for the basic scientist and the clinician as a curable human malignancy. However advanced disease at presentation contributes to poorer prognosis of these patients. It is suggested that extragonadal GCT must be kept in mind in differential diagnosis of a neck mass as the same could aid clinical outcome if attended to at an early stage.

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A Solitary Unilateral Astrocytoma of retina

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Abstract: *Tuberous Sclerosis is an inherited autosomal dominant syndrome, was first described by Bourneville in 1880 and was known as Bournville's disease until recently. The retinal involvement was first recognized by Vander Hoere in 1920. Solitary astrocytic hamartomas may be seen in otherwise normal individuals, but in patients with tuberous sclerosis they may be multifocal and bilateral. These tumors are also reported in association with neurofibromatosis.*

Key words:

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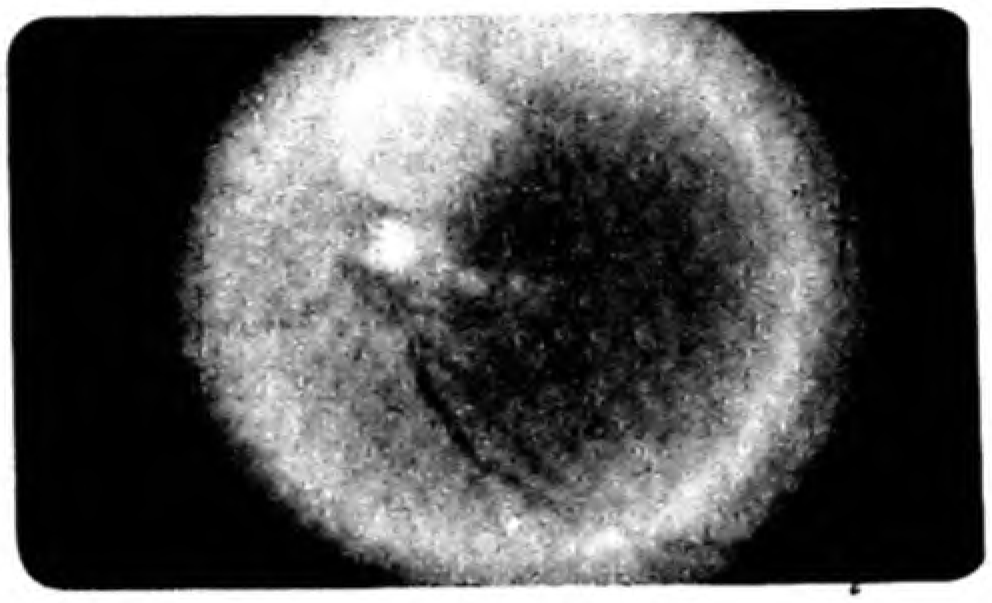
Case Report

A thirty five years old female came for a routine ophthalmic examination. Externally both eyes were clear and free of inflamation or irritation. The anterior segment was within normal limits. The intra-ocular pressure measured 15 mm Hg in both eyes. Fundus examination showed a large semitransparent yellowish sub-retinal mass in one eye in juxtaposition to the supero-temporal margin of the optic nerve head, extending 3 disc diameters temporally and 4 disc diameters vertically. The overlying and surrounding retina was attached. Numerous calcific spots were seen over the growth. No haemorrhage was present over the lesion, nor in the surrounding retina. Fundus examination of the other eye was normal. General physical examination of the patient did not reveal any sign suggestive of tuberous sclerosis. However, the appearance of fundus lesion was typical of solitary astrocytic hamartomas. The CT Scan of head was normal.



Discussion:

Tuberons sclerosis was first discovered by Bourneville in 1980. The retinal involvement in this condition was described by Vander Hoere[1]. The retinal lesions are of two major types (a) large, whitish (non-calcified) nodular masses (b) flat translucent (nor-calcified) smooth tumors[2] (c) intermediate type with features of both (a) and (b) types.[3]

Most astrocytic hamartomas occur at or near the optic disc. More peripheral solitary lesions are also seen and may be easily mistaken for retinoblastoma. Almost all astrocytic hamartomas of the retina in tuberous sclerosis are endophytic in nature. These retinal tumors are benign and non-neoplastic,[4] although progressive enlargement associated with the development of calcification has been reported.[5]

Ocular complications of hamartomas associated with tuberous sclerosis are rare and include vitreous hemorrhage, retinal vascular abnormalities including telangectasia, neovascularization, exudation and vitreous seeding.

Our case showed the features of a solitary large semitransparent yellowish sub-retinal mass in juxtaposition to the supero-temporal margin of the optic nerve head with numerous calcific spots over the growth, however, no signs suggestive of tuberous sclerosis were seen.

Summary and Conclusion

Solitary astrocytic hamartoma is a rare entity presenting as a sub retinal growth usually near the optic nerve head with no features suggestive of tuberous sclerosis.

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Ectodermal Dysplasia

Mushtaq Ahmad MD.; Wajid Ali MD.; K.M. Baba MD.; Masood-ul-Hassan MD.; Muzaffar Jan MD.

Abstract: *The term Ectodermal dysplasia is used to designate a heterogenous group of disorders characterised by a constellation of findings involving a primary defect of the teeth, skin and appendageal structures including hair, nails and sweat sebaceous glands.*

We report two cases of Ectodermal dysplasia in a family, brother and sister of hypohidrotic type.

Key Words: *Ectodermal, Sweat glands, Hypohidrotic, Dysplasias.*

JK Practitioner 1998; 5(4): 308-309

Case Report

3 years old female child and her younger brother 2 years old, born of a consanguinous marriage were admitted in our ward with similar complaints of on and off fever and generalised weakness and absent seating.

On Examination

Female Child's anthropometory weight was 12 kgs (expected 14 kgs) Head circumference : 50 cms, Height: 9cms (expected 95 cms) Mild pallor, pointed ears, sparse wispy hair, Frontal bossing, Sparse eye brows and eye lashes, peri-orbital hyper-pigmentation, mid facial hypoplasia pegged teeth, flat nasal bridge, coarse dry skin, hyperkeratosis with normal nails. (fig. I)

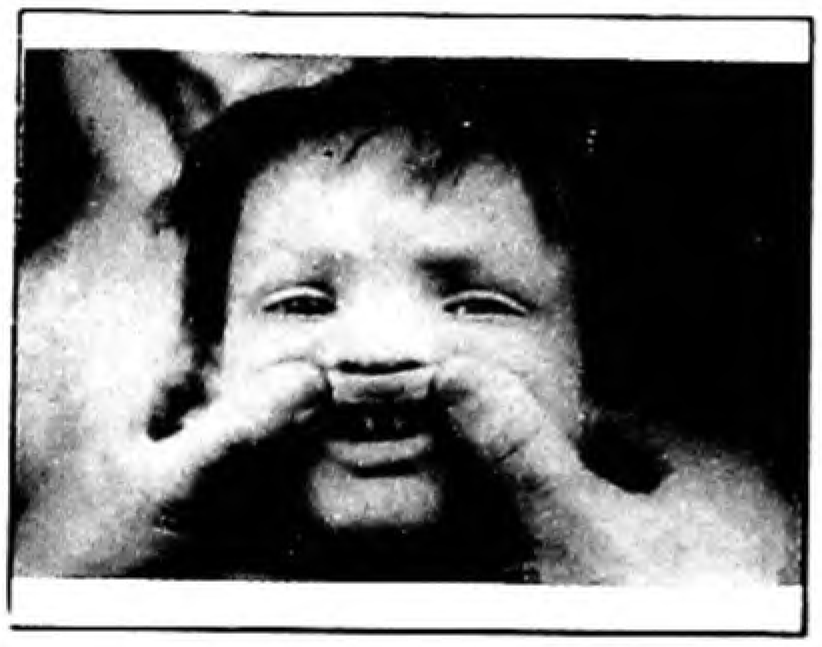

Fig-I

Systemic examination eye within normal limits. Investigations: Hb 9.5 gm%, TLC-6500/cumm, P 38%, L 58%, E 4% and PBF of hypochromic microcytic type. Routine urine and stool examination -Normal Blood urea 16mg%, Creatinine: 0.8mg%, Sodium: 131 meg Potassium 4.2meg, Sugar 90mg% Blood and urine culture - Sterile X-ray chest - Normal, Mantoux test-Negative. Skin biopsy: Consistent with Anhidrotic ectodermal dysplasia (Slide No. -1). Male: Wt. 11kgs, Head circumference 48 cms, Ht 85 cms.

General Examination

Mild pallor, pointed ears, sparse wispy hair, frontal bossing, Sparse eye brows and eye lashes, periorbital hyper-pigmentation, flat nasal bridge, mid facial hypoplasia, pegged teeth, Coarse dry skin, hyperkerotosis with normal nails. Systemic and eye examination was within normal limits. (Fig-II)

Investigations: Hb 10mg% TLC 7200/cumm, P; 40%, L:58% E-2% PBF: Hypochromic microcytic RBC's KFT, Suqar & electrolytes - Normal Urine and stool examination: Normal. Blood and urine culture-Sterile, X-ray chest-Mormal. Mantous test-Negative.

Skinbiopsy consistent with anhidrotic ectodermal dysplasia.

Discussion

Ectodermal dysplasia occurs as Hypohidrotic and Hidrotic varieties. Hypohidrotic (Anhidrotic) type: This syndrome manifests as a trial of defects. Partial or complete absence of sweat glands, anamolous dentititon and hypotrichosis.[1] It is usually inherited as X-linked recessive trait, with full expression in males only, however, any autosomal recessive mode of inheritance may be operative in some families.[2] Heterozygous females have no or variable clinical manifestations because of random X-inactivation. Affected children are unable to sweat, have high fever in warm environment and may mistakenly be considered as having fever of unknown origin. This is particular in infancy, when facial changes are not easily

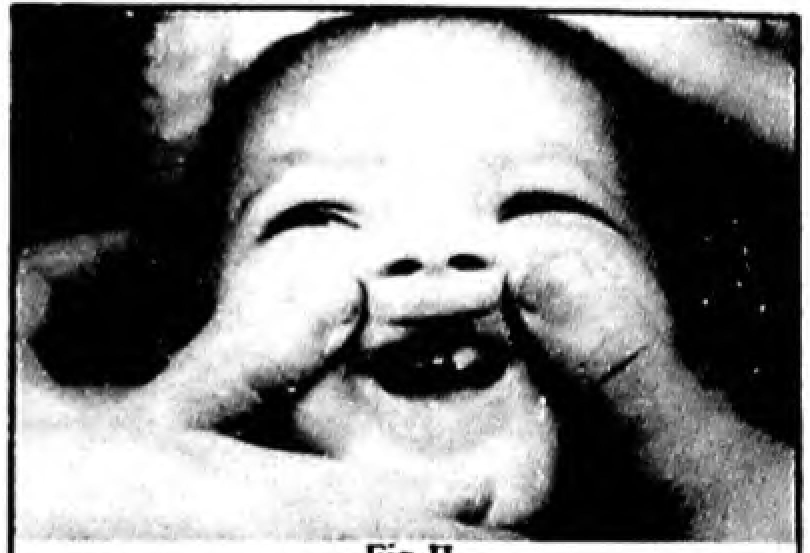

Fig-II

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appreciated. The typical facies is characterized by frontal bossing, malar hypoplasis flattened nasal bridge, wrinkled and hyperpigmented periorbital skin and prominent low set ears. Skin over entire body is dry and extensive peeling of skin is clinical clue in newborn period. The paucity of sebaceous glands may account for the dry skin. Hair is sparse, curly and hypopigmented and eye brows and lashes may be sparse or absent. Anodontia or hypodentia with widely spaced conical teeth is a consistant feature. Less commonly stenotic laminal puncta, Corneal spacity and catar acts are observed.

Incidence of atopic disease in children is relatively high. Poor development of mucous glands in the respiratory and GI tract result in increased susceptibility to respiratory infection, purulent rhinitis, dysphonia, dysphagia, and diarrhoea. Sexual development is normal. About 30% males die during first two years of life of hyperpyrexia or respiratory infection.

Sweating deficit, a reflection of hypoplasia or absence of eccrine gland may be documented by pilocarpine iontophoresis and is diagnosed by palmar skin biopsy.[3]

Treatment of these children includes protecting them from exposure to high ambient temperatures, early dental evaluation and prosthesis for cosmetic purposes, use of artificial tears in case of defective lacrimation and wearing of wig if alopn necessiates.

Hidrotic (Clouston) type

Dystrophic, hypoplastic or absent nails, sparse hair and hyperkerotosis of palms and sales are salient features of this variety.

Sweating is always normal, dentition is usually normal and the disorder is inherited as autosomal dominant.

EEG Syndrome:

Ectrodactyle (Split hand and foot), ectodermal dysplasia, cleft lip and palate and tear duct abnormalities constitute the EEG syndrome, which is inherited as autosomal dominant trait of variable expressivity. Two other rare varities are Rapp Hodgkin and Robinson, Dysplasias, Sensineural deafness, growth deficiency hypospadias are seen in these types.

In our patients, all the clinical features and skin biopsy confirm the diagnosis of Hypodrotic (Anhidratic) ectodermal dysplasia. One male and another female sib being affected go in favour of autosomal recessive inheritance. Parents were clinically normal.

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Cloacal Exstrophy - A Case Report and Review of Literature

Akash A Shah MBBS.; Baldev S. Wazir MS.; Shabeer A Wani MBBS.; M. Ayub Bhat MBBS.; Ab. Khaliq Sheikh MS.; Shabeer H. Shah MBBS.

Abstract: *A case of cloacal exstrophy is reported here, first time in Kashmiri population. A neonate 6 hours old, having four gut orifices and two hemibladders alongwith undescended testis and bifid penis representing classical features of cloacal exstrophy was referred to our hospital on 21.06.1997. First stage operation was performed but patient finally expired on 7th post-operative day. This challenging abnormality is correctable nowadays, but there should be close coordination between orthopedician, urologist, peadiatric surgeon, neonatologist, physiotherapist, social worker, nutritional supporting unit and intensive care nurse.*

***Key words:** Cloacal Extrophy, Ventral Abdominal wall defects.*

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Introduction

Cloacal exstrophy also referred as vesico-intestinal fissure, ectopic cloacal, ectopia viscerum, complicated exstrophy of bladder and abdominal fissure is the most severe form of ventral abdominal wall defects. They consist of an omphalocele superiorly and exposed bladder and bowel inferiorly. The bladder is bivalved in the mid-line by a zone of intestinal mucosa with each hemibladder containing a ureteral orifice. The exposed intestinal mucosa that sits between the hemibladders histologically represents the ileocecal area. It may contain upto four orifices. The most superior orifice represents the proximal bowel. Whereas most inferior orifice represents distal bowel. The distal bowel orifice is actually the hindgut which ends in a blind pouch and is associated with an imperforate anus. One or two appendiceal orifices are found between the proximal and distal bowel orifices (Fig I). Genital abnormalities are found in all cases. In males, undescended testis are present. The penis is usually bifid with each half epispadic and attached to widely separated pubic rami.[1] In females the clitoris is divided and usually associated with a duplex vagina and bicornuate uterus.[2]

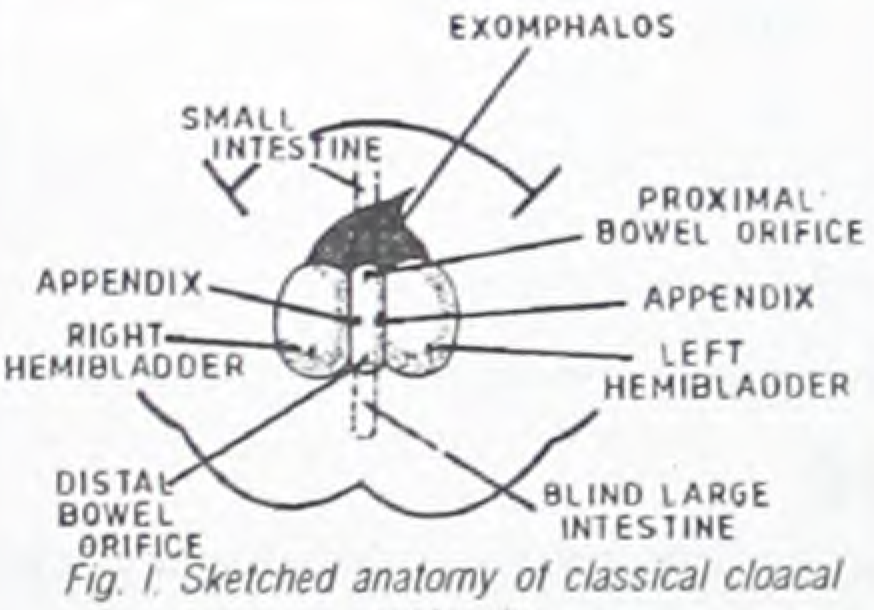

Fig. I. Sketched anatomy of classical cloacal exstrophy

Case Report

A six hours old male neonate born as full term normal delivery, product of non consangious marriage, second in birth order was referred to urological division of our hospital for evaluation and management of ventral abdominal wall defect with exposed viscera on 21.06.1997. The first sibling of this baby was normal with no congenital anomaly. The medical histories of both parents were insignificant. The examination revealed low birth wight (2.1Kg) baby with no signs of prematurity having normal neonatal reflexes. His pulse rate was 142/min regular, respiratory rate of 48/min with no icterus, cyanosis or pallor. Chest and cardiovascular system were clinically normal.

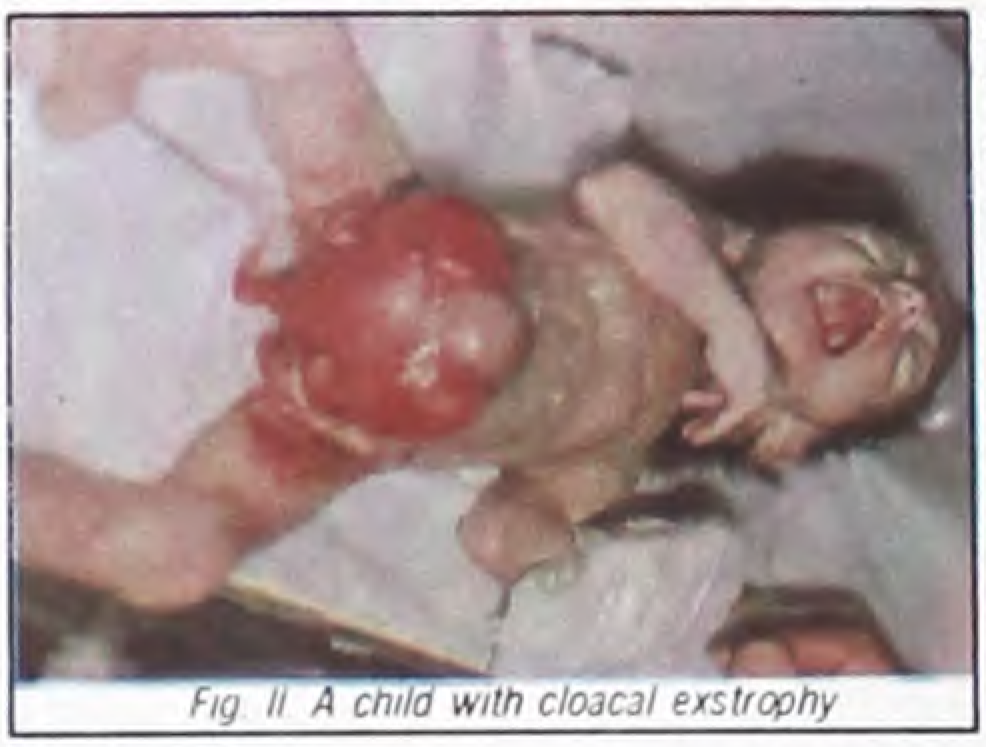

Fig. II. A child with cloacal exstrophy

Local examination revealed ventral abdominal wall defect with an omphalocele, two hemibladders and four gut orifices. There were two appendices, one being visible and other seen on exploration. There was also bifid penis with undescended testes (Fig 2).

Neonate was shifted to neonatal intensive care unit and kept in an incubator. Routine laboratory studies were performed and showed Hb 16 gm%, TLC 6.3x10^9/L, DLC P69% L31% and platelets 181x10^9/L. His serum

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electrolytes, blood glucose, BUN, serum creatinine, serum calcium, liver functions, urine analysis, chest radiograph were all within normal limits. 100ml. of blood was arranged after typing and cross matching. An I.V. line was started with N/5 saline in dextrose 10% along with postassium supplements. After initial resuscitation it was decided that baby will be taken for first stage procedure (detailed in discussion).

Inj. Ceftriaxone 200mg I.V. stat was given 30 minutes before surgery and the baby underwent first stage repair under general anaesthesia uneventfully. Post-operatively neonate was put on mechanical ventilator and weaned off it on 4th post-operative day.

Unfortunately on 5th post-operatively day baby developed signs of respiratory tract infection, leading subsequently to gram negative culture positive septicemia, forcing us to put him again on mechanical ventilation and I.V. antibiotics as per culture report. But baby finally expired on 7th post-operative day.

Discussion

Cloacal exstrophy was first described by Littre in 1709[3] and first successful reconstruction was reported by Rickham in 1960.[4] It occurs in 1 in 120,000 births. Males are slightly more affected than females.[5] This abnormality is considered a manifestation of abnormal embryogenesis rather than an arrest in development. Two main theories explain this abnormal embryogenesis. The "caudal displacement theory" suggests that caudal displacement (caudal to anal portion of cloaca) of the paired primordia of the genital tubercle, relative to the point where the urorectal fold divides the primitive cloaca into the urogenital and anal components, explains the genesis of this anomaly.[6]

The other main theory proposed to explain the development of cloacal exstrophy is the "wedge effect" of an abnormally large cloacal membrane.[7] We support this theory because an abnormally large or a persisting cloacal membrane acts as a wedge to developing structures of the abdominal wall with rupture of this unstable membrane prior to descent of the urorectal septum and fusion of genital tubercles, resulting in a midline infraumblical defect, exposing bladder and bowel mucosae and producing bifid external genitalia. The associated anomalies of cloacal extrophy occur in upto 85% of patients.

Abnormalities of the upper urinary tract are most common and include pelvic kidney, hydronephrosis/ hydroureter, uretericatresia, unilateral agenesis, multicystic kidney, ureteralduplication and crossed fused ectopia. The most common vertebral anomaly is myelodysplasia. The survivors have normal intelligence.[9] Other abnormalities include gastrointestinal, abnormalities of lower limb, omphalocele, abdominal wall deficiency, absent or double vas, imperforate anus, scoliosis etc.[10]. The emergency surgical correction is neither wise nor indicated in these patients. The most important issue is gender assignment and majority of males with cloacal extrophy should be rared as females. So in male infants who are assigned to the female gender orchiectomy should be performed at the time of initial reconstruction. Presently antenatal detection of cloacal exstrophy is possible by utilizing ultrasonography.[11]

For surgical correction high family support and their consent for whole plan cannot be over-empahsized. In general the first operative stage consists of, closure of omphalocele; separation of intestinal plate from the hemibladders with construction of gastrointestinal stoma; reapproximation of separated bladder halves, if possible; and orechiectomy to assign to the female gender. Additional procedure like neurosurgical, orthopedic etc. may also be performed at the same time.

The second or major operative stage is usually performed when infant gains a weight of 8-10 kg, the patient should be thriving and at a reasonable operative risk. The surgeries performed include reconstruction of bladder and/or urethra as well as the external genitalia.

Conclusion

This case report emphasizes that infants with this devastating complex malformation should not be allowed to die, although the emotional, physical and economical handicaps are too great and mortality rates are very high. The fortunate thing for these patients is that if they survive they have mild neurological deficits, having the potential for fully functional, happy and productive life.

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Suicidal Poisoning in a Case of Gunther's Disease

G.Q.Khan MD; FCCP; Gh. Mohi-ud-Din MD; Tanveer Masood MD; G.H.Hajini MD; Dilshad Akhtar MD.

Abstract: *Congenital erythropoietic porphyria is an autosomal recessive, disorder also known as Gunther's disease, which is associated with hemolytic anemia and cutaneous lesions. Being a chronic debilitating disease the patients are prone to sucidial tendencies. A case of Gunther's disease, the first from SMHS Hospital, Srinagar, Kashmir is reported below. The patient having tried to commit sucide with organophosphorous compound.*

***Key words:** Gunther's disease, cutaneous photosensitivity, porphyria.*

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Case Report

A 27 years old women presented to S.M.H.S. Hospital with features of Organophosphorus poisoning. Patient was brought to Hospital in a Comatose state. There was an alleged history of organophosphorus poison ingestion. She had constricted pupils, gross fasciculations and excessive salivation. She was treated for Organophosphorus poisoning and after she became well, a detailed history was taken from the attendants which revealed that she passed red coloured urine since her birth. Also since her childhood, there was history of recurrent blistering lesions of skin, photosensitivity, hyperpigmentation of face and distal parts of both upper and lower limbs and mutilation of fingers. There was also history of excessive growth of hair on face for last three years. On general physical examination she had pallor, hyperpigmentation of face, distal parts of both upper and lower limbs, hirsustism, erythrodontia and mutilation of fingers and toes. Systemic examination revealed only splenomegaly.

Family history revealed that the patient was a product of consaguinous marriage. She had three sisters and two brothers. Her brother who was three years elder to her, also had the history of passing red colour urine since birth. He also had history of recurrent blistering lesions of skin, photosensitivity, hyperpigmentation of face and distal parts of both upper and lower limbs and mutilation of fingers. On general physical examination in addition to hyperpigmentation, erythrodontia, skin lesions and mutilation of fingers as those of her sister and he had corneal ulceration of right eye. Patients previous medical records rervealed that her urinary analysis was positive for urinary uro-and copro-porphyrins, and was labelled as a case of Gunther's disease.

Laboratory studies revealed anaemia with a haemoglobin Hb 8.7 gms/dl, PBF revealed hypochromic microcytic anaemia. Total leukocyte count, Differential leukocyte count, BT, CT, platelet count, ESR, blood sugar, kidney function tests, liver function tests, reticulocyte count, routine urine examination and CSF examination were normal. Porphobilinigen in urine was absent. ECG showed sinus tachycardia. Chest X-ray, bone marrow examination and C.T. scan Brain were of normal study.

Discussion:

Congenital erythropoietic porphyria, an exceedingly rare hereditary disease was first reported in 1874.[1,2] It was orginally named haematoporphyria congenita by Gunther in 1911. It was Mathias Petry in whom Gunther's disease was first described.[3] In India first report of this disorder was in 2 siblings reported by Taneja et al.[4] Both sexes are equally affected.[5] Nearly all cases begin in childhood and only a few in adult life, with one patient experiencing the first symptom at the age of 54 years.[7] Parental consanguinity has been reported[4,8,9] and so the occurence of disease among siblings suggested an autosomal rescessive mode of transmission[4,10-12]. Cutaneous photosensitivity is usually severe and begins early in infancy. The skin over sun-exposed area is friable with vesicles, which are prone to rupture and infection. Later there is mutilating deformity of hands, ears, face and nose. Patients may develop hypertrichosis and hyperpigmentation.[13] Patients pass pink red urine. There is usually erythrodontia, splenomegaly and haemolytic anaemia. Other clinical findings include eye changes e.g.,

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photophobia, keratoconjuctivitis, ectropion and symblepheron.[3] Under Wood's lamp the teeth exhibit a reddish pink flourescence.

Being a chronic debilitating/mutilating disease, Gunthers disease patient are prone to depression and suicidal tendencies. Other diseases where depression is common are Huntington's chorea, multiple sclerosis, parkinson's disease, cushing's disease. Addison's disease, hypothyrodism, apathetic hyperthyrodisim and rheumatoid arthritis[14] etc.

This patient had hyperpigmentation of face and distal parts of both upper and lower limbs, hypertrichosis, erythrodontia and mutilation of fingers and toes. She was so much depressed due to the stigmata of the disease itself, that she tried to commit suicide. This is the first case reported at S.M.H.S. Hospital where a patient with an organic disease like porphyria has attempted to commit suicide. To the best of our knowledge this is the first reported case of suicide in a Gunthers disease in our state.

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Tension Pneumopericardium Following Blunt Thoracic Trauma- A Rare Phenomenon

Ghulam Nabi Lone, M.Ch; Rajendar Kumar Suri F.A.M.S., F.I.A.C.S.;
Shyam Kumar Singh Thingnam, M.Ch.; Neerod Kumar Jha, M.Ch, D.N.B.

Abstract: *Pneumopericardium sufficient to cause cardiac tamponade is an uncommon entity. We present a patient who had sustained chest trauma during a vehicular accident. He developed rapidly progressive cardiac compressive shock. Diagnosis was established by radiography, substantiated by strong clinical suspicion of hemopericardium. Left anterior minithoracotomy proved to be life saving.*

Key words: *Pneumopericardium, Cardiac tamponade, Cardiac compressive shock, Minithoracotomy.*

JK-Practitioners 1998; 5(4): 314-315

Indroduction

Usually cardiac tamponade in pneumopericardium is caused by penetrating trauma. It rarely has been seen in closed chest injury[1]. The diagnosis calls for high index of suspicion of the possibility and has a great relevance to the experience of the attending clinician. Shackelford[2] published reports of 9 patients with pneumopericardium following closed chest trauma. Hudgens[3] reported two cases of tension pneumopericardium following blunt thoracic trauma. Mirwis[4] reported 4 cases with radiological evidence of pneumopericardium and "small heart" sign. We report another case of tension pneumopericardium with the similar mechanism.

Case Report

36 yrs old male, alcoholic, was brought to emergency ward with the history of blunt trauma in an automobile accident. He was tachypneic, with a respiratory rate of 36/mt. Pulse rate 110/min and blood pressure of 70/40 mmHG. Chest examination revealed a chest wall hematoma near lower left parasternal area with local subcutaneous emphysema. Hamman's crunch was obvious. Heart sounds were muffled. Air entry was reduced on left side. Paracentesis thoracis was negative on both sides. EKG was low voltage type. Chest x-ray showed gross pneumopericardium and minimal pneumothorax on left side. Cardiac silhouette was reduced. There was no bony injury. Blood gas analysis revealed pH of 7.28, $PaCo_2$ of 50 mmHg and PaO_2 of 72 mmHg. Bronchoscopy was normal. Tube thorocostomy was undertaken immediately under local anaesthesia but without any improvement in the hemodynamic status and the left lung did not expand for 12 hours. Exploration during minithoracotomy revealed a contusion over the pericardium near diaphragmatic region but intact pericardium otherwise. The patient improved dramatically after pericardiostomy. Pulse rate decreased to 90/ mint. and Blood pressure increased to 130/70 mmHg. Intercostal tube was removed after 48 hours and patient discharged after 5 days.

Discussion:

The etiology of pneumopericardium varies widely. The commonest factor happens to be the penetrating trauma.[1] The mechanism of pneumopericardium with blunt chest injury begins with sudden increase in intrathoracic pressure, producing alveolar rupture. Thus, the air released finds its way into the pleural cavity as pneumothorax.[1]

Pneumopericardium is produced by way of pleuro-pericardial communication as a result of associated pericardial tear[5,9] or frank pericardial rupture.[6] However, congenital rents in pericardial sac may also persist.[3] However, if the visceral pleura is intact, in that case air may enter into the interstitial space and can traverse along the perivascular planes of the pulmonary vessels into the pericardium.[1,5,7,8]

Positive pressure breathing exacerbates the leakage of air from ruptured alveoli, resulting into pneumothorax and pneumopericardium[1]. Direct apposition of tracheobronchial and pericardial tears has been postulated.[5,12]

Our patient had significant local surgical emphysema over the left anterior chest. Tube thoracostomy did not decompress the pericardium. Pneumothorax on the left side persisted. Peroperatively the pericardium was intact and the left lung was contused minimally over the lingula. Visceral pleura was intact otherwise. The most plausible mechanism was the dissection of air along the pulmonary interstitium. The patient had a dramatic relief with pericardiostomy.

Diagnosis depends on the clinical opinion and the radiography. Examination reveals muffled heart sounds.

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Table 1. Patients with tensión pneumopericardium following blunt thoracice trauma-clinical characteristics

Authors	Age/sex	Mechanism of injury	Tracheo-bronchial rupture	Pneumo-thorax	Other injuries	Mechanical ventilation	Treatment	Outcome	Cause of death
1. Westaby[5]	23/M	MVC	Yes(Rmb)	Yes	SCE	Yes	Thoracotomy	Survived	-
2. Mc Doungal[8]	12/M	MVC	No	No	Pnmd, Scapular fracture	Yes	Pericardio-centesis	Survived	-
3. Mirwis et al[4]	14/M	Explosion	No	Yes	SCE, pnmd, LC, ARDS	Yes	SPW	Died	MOF
	18/M	MVC	No	Yes	SCE,Pnmd, LC, ARDS	Yes	SPW	Died	MOF
	17/M	MVC	No	Yes	LC, ARDS,	Yes	SPW	Unknowr.	-
	18/M	MVC	Yes(RMB)	Yes	Flail chest,	Yes	SPW	Died	HI
4. Osionowo and Adebo11	35/M	MVC	No	No	SCE,LC	No	Pericardio-centesi	Died	Unclear
5. Gupta10	24/M	MVC	No	No	Pnmd	No	-do-	Survived	-
6. Hudgens et al3	17/M	MVC	No	Yes	LC	Yes	SPW	Survived	-
	16/M	MVC	No	Yes	LC	Yes	SPW	Survived	-
7. Capizzi et al1	25/F	MVC	No	Yes	SCE,Pnmd,	Yes	SPW	Died	ARDS
8. LOne et al	36/M	MVC	No	Yes	SCE,LC	No	Thoracotomy	Survived	-

Hamman's crunch, palpable crepitus of surgical emphysema and hypotension. Radiography reveals an hypertranslucent outline of heart, separated from lung field by the pericardium sparing the superior mediastinum unlike pneumomediastinum[1]. Mirwis[4] has reported diminished cardio-thoracic ratio in tension pneumopericardium. However "small heart" sing developed late in our patient. An upright chest x-ray film may demonstrate a horizontal lucency in the transverse sinus on posterio-anterior projection or a lucent triangle anterior to the cardiac base and aortic root on latyeral projection[1]. Pericardial air will shift with changes in position for decubitus films.

EKG may show low voltage pattern, suggestive of cardiac tamponade. Echocardiographic findings of pneumopericardium have been described but are not different from those of pneumomediastinum- "air gap sign"[1].

The literature of 12 blunt trauma patients was reviewed[1]. Two patients had tracheo-bronchial injuries and 9 had pneumothorax. 9 of 12 patients were mechanically ventilated prior to surgical intervention for tamponade. Iatrogenic baro-trauma contributed to the development of tamponade in these patients, as only 6 of the 20 patients with tamponade were mechanically ventilated. Sub-xiphoid approach was the most common route for decompression and mortality was 41.6%[1] (Table-I). However, we performed left antero-lateral minithorocotomy and morbidity did not get affected.

Emergency pericardiocentesis is of paramount importance following rapid fluid resuscitation[8,10,11]. However, in case hypotension perisists, patient shouljd be undertaken for surgical intervention in the form of sub-xiphoid pericardiostomy or emergency thoracotomy[5].

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Hemihypertrophy In A Child

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Abstract: *A rare case of hemihypertropy involving right side of body in a 6 year old male child is presented. Detailed work up and periodical surveillance failed to reveal any associated anomaly or appearance of Wilms tumour. Pertinent literature is reviewed briefly to highlight the various possible anomalies/tumours associated with patients of hemihypertrophy.*

Key words: *hemihypertrophy, wilms tumour.*

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Case Report

A 6 year old male child presented with a progressive overgrowth of right side of the body since birth. However, the parents were more perturbed about the facial asymmetry. There were no other complaints. Family history was negative regarding the present problem or associated traits of aniridia, Wilms tumour. On examination the child seemed to have normal intelligence as per his age. The right side of the face including the right ear was overgrown. Also, the overgrowth of the right lower and upper limb was very obvious. Although there was difference in the size of right chest and abdomen compared to the contralateral side, it was not so obvious (fig.1). External genitals were normal. A detailed workup (Blood sugar, chest X-ray, US abdomen, Karyotype) was normal, suggesting that the hemihypertrophy was affecting the musculo-skeletal system only. The child remains free of any tumour occurrence (Wilms, Adreno-cortical) after 4 years of follow up.

Discussion

Hemihypertrophy is a rare clinical entity and its exact incidence and cause is not known[1]. These patients have an increased incidence of Wilms tumour, adrenocortical tumours, hepatoblastoma, mental deficiency, club foot-syndactyly, congenital heart disease, cryptorchidism and hypospadias[2]. Of these Wilms tumour is more common and may occur in 3% of the patients of hemihypertrophy and it may occur on the contralateral side[3]. This association seems to be non-heritable as compared to aniridia where it is heritable with chance of Wilms tumour as high as 33%[3]. Occasionally hemihypertrophy is associated with Beckwith-Wiedemann syndrome at birth or develops later on. These babies are more prone to develop tumours as compared to those having isolated hemihypertrophy[4]. Going by the above facts, it seems highly prudent to have close follow up in patients of hemihypertrophy to detect the development of tumours (Wilms, Adrenocortical, Hepatoblastoma) at the earliest. The most effective method of surveillance of these children is by abdominal ultra-sonography every three months unitl the child is 2 years old and every 6 months until the age of 6 years[5].

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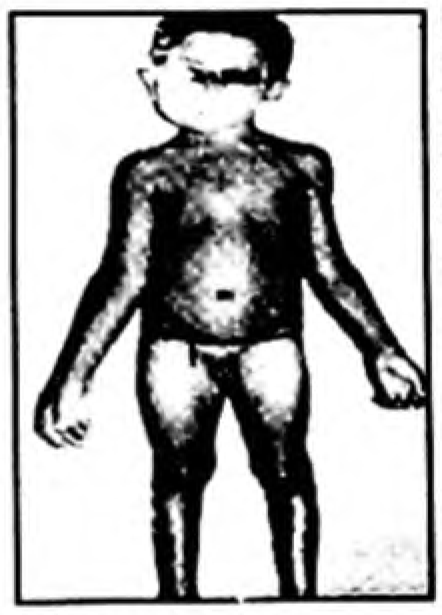

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Seroprevelence of Brucellosis in Kashmir (India) among patients with pyrexia of unknown origin

Brucellosis is a systemic bacterial disease characterised by a multitude of somatic complaints but with a paucity of physical findings. The most frequent symptoms of acute brucellosis are fever, sweating, especially natural, weakness, malaise, myalgias, backache and anorexia. Most notable findings are hepatosplenomegaly and lymphadenopathy. Fever is almost invariably present and shows waxing and waning pattern (Undulant fever). Characteristically in brucellosis fever rises in a ladder like pattern through a week to 10 days to 39°C or 40°C and then a gradual fall to normal over another week and the cycle is repeated every 2-4 weeks. However in the abscence of any localizing signs patients easily may be diagnosed as Pyrexia of Unknown Origin (PUO). Since the most common cause of PUO especially in developing countries is infections, the present study aimed to see the role of brucellosis in causing PUO, in patients hospitalised in Kashmir.

The study was conducted in the Department of Microbiology Govt. Medical Srinagar, Kashmir (India) and included 3,532 patients undergoing evaluation of pyrexia of unknown origin over a period of five years from 1992-1997. The patients were referred to the department from various medical units of Govt. Medical College hospital (650 beded teaching hospital) and catering to approximately 60 percent of total population of Kashmir (Total population around 6 million). All these patients were investigated for serological evidence of brucellosis. Wright's tube agglutination test (TAT) was the serological test performed.

Out of the 3,532 patients with PUO subjected to sero diagnosis for brucellosis using TAT. 28 (o.8%) tested positive for brucellosis (a titer >1:160). Of the 28 patients who tested positive for brucellosis there were 21 males and females with a male female ratio of 3:1. The most common age group involved was 21-30 years (42.8%) andf the least common age group involved was 10-20 years (3.5%). The higher involvement of the 21-30 age group was completely attributable to male patients. The female patients were equally distributed over the various age groups. About half of the patients had a titer of 1:160. Higher titers of 1:256, 1:320, 1:520 and 1:1024 were observed in respectively 6,1,3 and 3 patients.

Brucellosis is a major zoonotic infection caused by one of the three species of genus Brucella pathogenic in human. Brucellosis exists worldwide especially in countries of Arabian gulf, Mexico, Central and South America and the Indian subcontinent. Becuase of the animal origin of human brucellosis there is a strong occupational predisposition and affects adult men coming in contact with animals or animal products. The consumption of raw milk and milk products forms another important risk factor[1,2]. In India Patil and Coworkers[3] in their study reported 160 patients of brucellosis with a male to female ratio of 3:2. In our study males outnumbered females by a ratio of 3:1. This goes with the reported trend world wide. However a recent study from the Kingdom of Saudi Arabia showed a higher incidence in females between 15 to 64 years. Above 65 years males had higher incidence.[4]

There is paucity of literature on brucellosis causing human disease, including Pyrexia of Unknown Origin (PUO) for the Indian subcontinent. Sharma and Coworkers in their study conducted in two northern states (Utter Pradesh and Delhi) of India noted a seroprevelence of 0.9% in man.[5] They also reported percentage of seropositivity of brucellosis in animals as: goats 5.5%, sheep 3.4%, pigs 16.0%, cattle 6.4%, Buffalo 4.9% and 12.8% in horses. Nawathe and Coworkers in their study conducted in the Central Indian region of Nagpur reported a bovine seroprevalence of brucellosis as 9.7%.[6] Panjarathinam and Coworkers studied 805 women with spontaneous abortion. Fifty two (6.5%) of these women were seropositive for brucellosis. This study was carried out in a rural farming Community of Ahmedabad (India) with low socio economic status and contact with animal.[7] The present study shows a Seroprevalence of 0.8% among patients hospitalised with PUO indicating that this often severe disease is an important cause of morbidity.

Since India has a population of over 900 million, with 80% living in rural area, with farming as the commonest occupation and with occupational contact with livestock as a major risk factor, the role of Brucella in causing disease in human in India has not been studied enough.

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Cutaneous Manifestation after Lithium

Lithium was discovered by Arfwedson in 1818. Known for its calming effects in Roman times, lithium salts have recently been used to treat mania. Cade. J [1] reported its antimanic effects and same got approved officially by food and drug administration in 1970. Lithium manifests morphogenic effects on various tissues of the body. Its effects on kidney have extensively been investigated since it is mainly excreted through kidneys. Its cutaneous effects in the form of folliculitis[2] exfoliative dermatitis[3] and exacerebation of psoriasis[4] have been observed from time to time.

Twenty albino rats weighing 150 gms on an average were used during present study. The animals were grouped in A and B groups. Five animals in former group received usual food and plain water and served as control, whereas 15 animals in group B were fed with therapeutic doses of lithium carbonate in addition to usual food and drinking water. The drug was mixed with flour and was fed to animals in the form of pallets. The process of drug adminstration continued for 90 days regularly. The tissues obtained were processed manually for block making. Blocks were subjected to routine technique and slides thus prepared were stained with haematoxyline and eosin for microscopic study.

Microscopically the cutaneous lesions observed after lithium therapy during 90 days of study included atrophic changes in epidermal layers and hypercollagenation of dermis. Besides sections also revealed proliferation of sebaceous and sweat glands. In addition desquamation of cutaneous surfaces in scales and infiltration of dermis by histeocytes and fibroblasts were also observed.

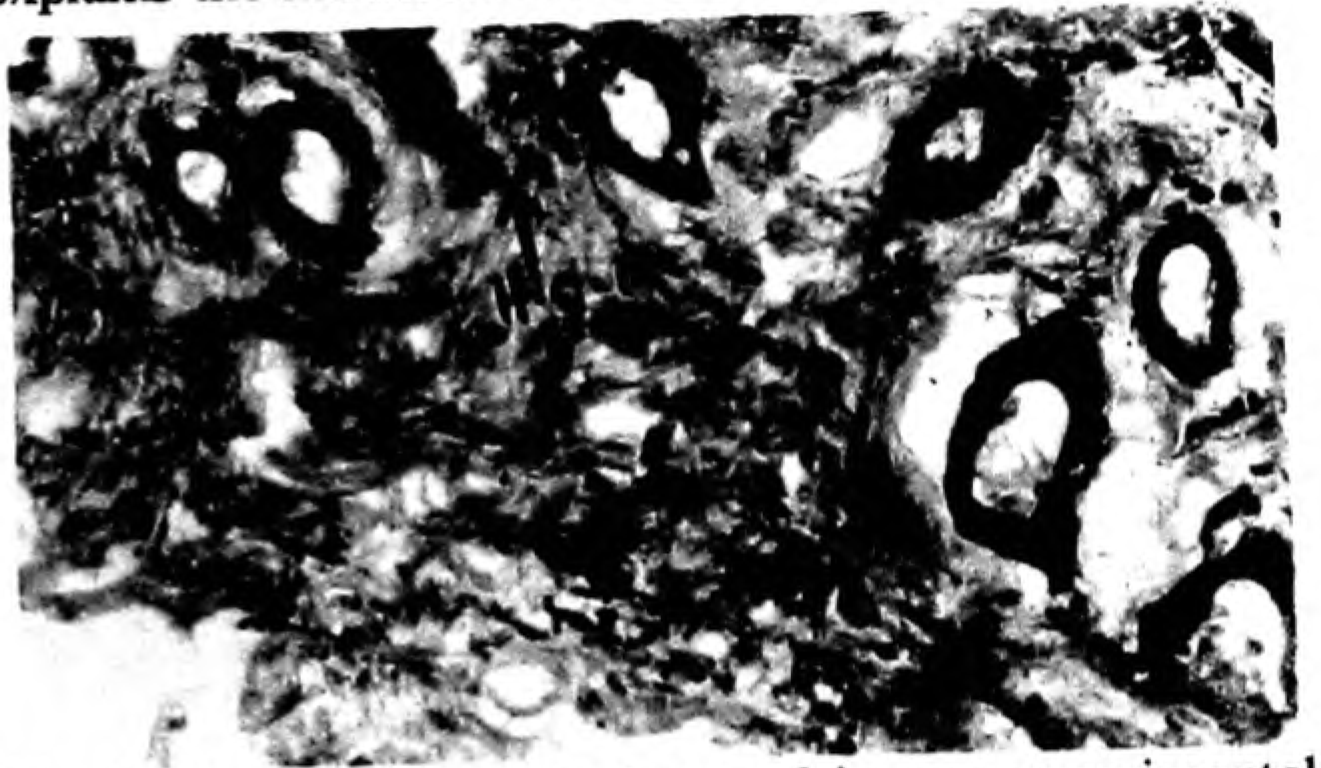
The dermatological side effects resulting from lithium adminstration have been well documented. There is divergent opinion regarding the effects of drug on skin. Some believe it to be toxic and others opined it to be of allergic nature.

The cutaneous side effects were first described by Callaway[5]. Psoriasis as a side effect of lithium was first reported by Carter[6] and later by Skott and his associates[4].

Khunley et al[3] reported the occurance of exfoliative dermatitis followed by desquamation of skin. Kurtin B [7] also described folliculitis after lithium therapy.

During 12 weeks of present study, lithium fed rats showed atrophic changes in epidermal layers. In addition there was also hypercollagenation of dermis and proliferation of sebaceous and sweat glands. The dermis also showed round cell infiltration at places.

The pioneer work by Reifers J et al[8] by using flame spectrophotometry stated that lithium gets accumulated in epidermis, dermis and adipose tissue. This statement explains the menifestations on the skin associated with histological changes as observed in our experimental work.



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JK-Practitioner 1998; 5(4) : 322

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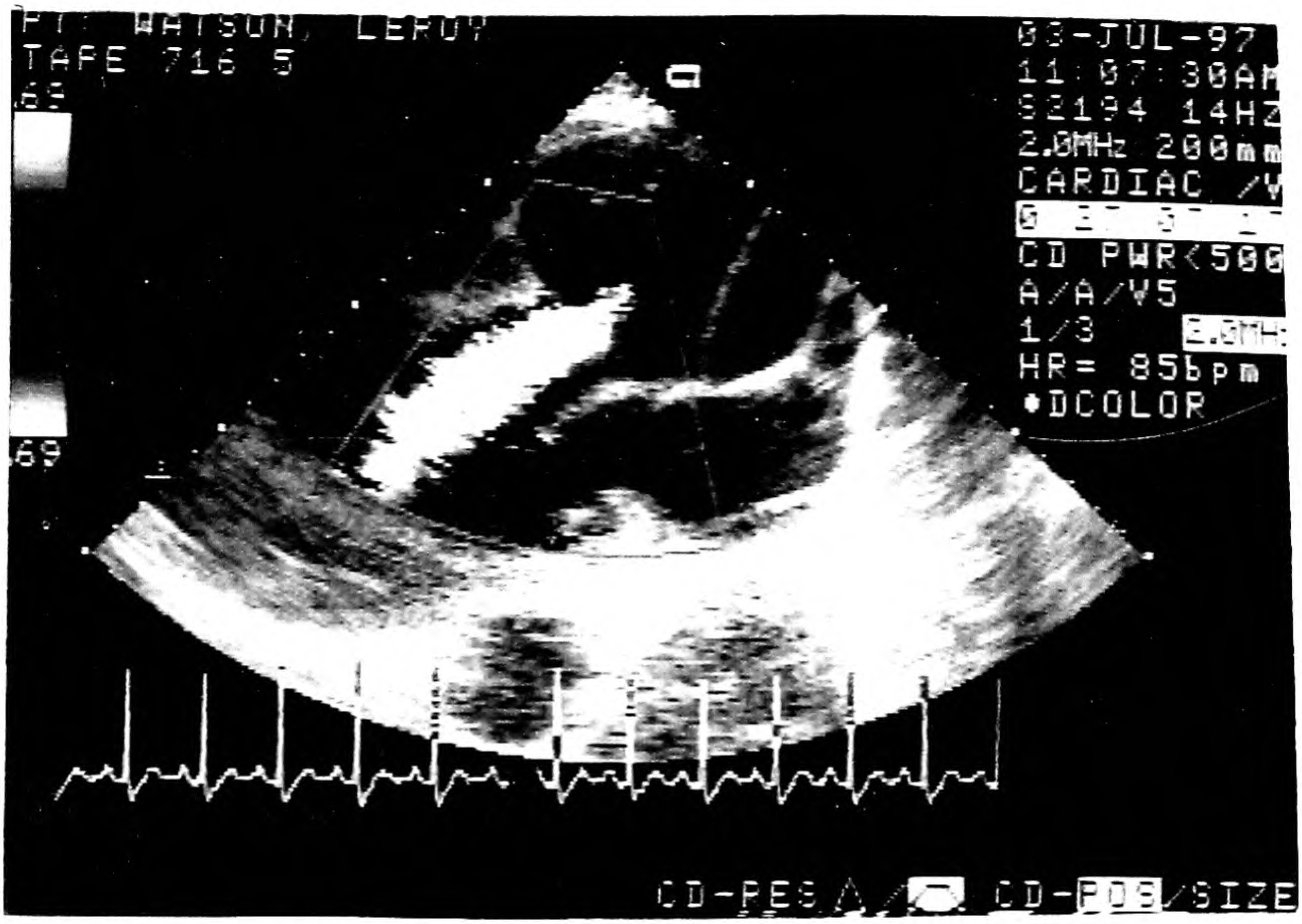
Painless Aortic Dissection in Marfan Syndrome

Mohammed Saleem MD, Riyaz Bashir MD, Faroque A Khan MACP



A 39-year old African American male with past history of hypertension presented with complaints of shortness of breath, paroxysmal nocturnal dyspnea and swelling of lower limbs for one week. Denied any history of chest, back or abdominal pain. On physical examination he had obvious marfanoid habitus with blood pressure of 155/60 which was equal in both the arms. Pulse rate was 100 bpm and regular with visible hyperdynamic carotid pulsations. Cardiovascular exam revealed a loud systo-diastolic murmur in the aortic area, which was associated with a thrill. Rest of the physical examination was unremarkable except mild to moderate peda; edema. Electrocardiogram revealed cardiomegaly, tortuous aorta and clear lung fields. A transthoracic echocardiogram showed severe aortic and tricuspid regurgitation. In addition it revealed marked aortic root dilatation with dissection (Figure). A CT scan showed extension of dissection to aprtic bifurcation. Patient underwent emergent surgery (Bentall's procedure with aortic valve replacement, as a part of multiple stage repair of the aorta).

This case illustrates that *patients with Marfan syndrome need serial echocardiographic follow-up of their aortic root diameter and presence of painless dissection.*

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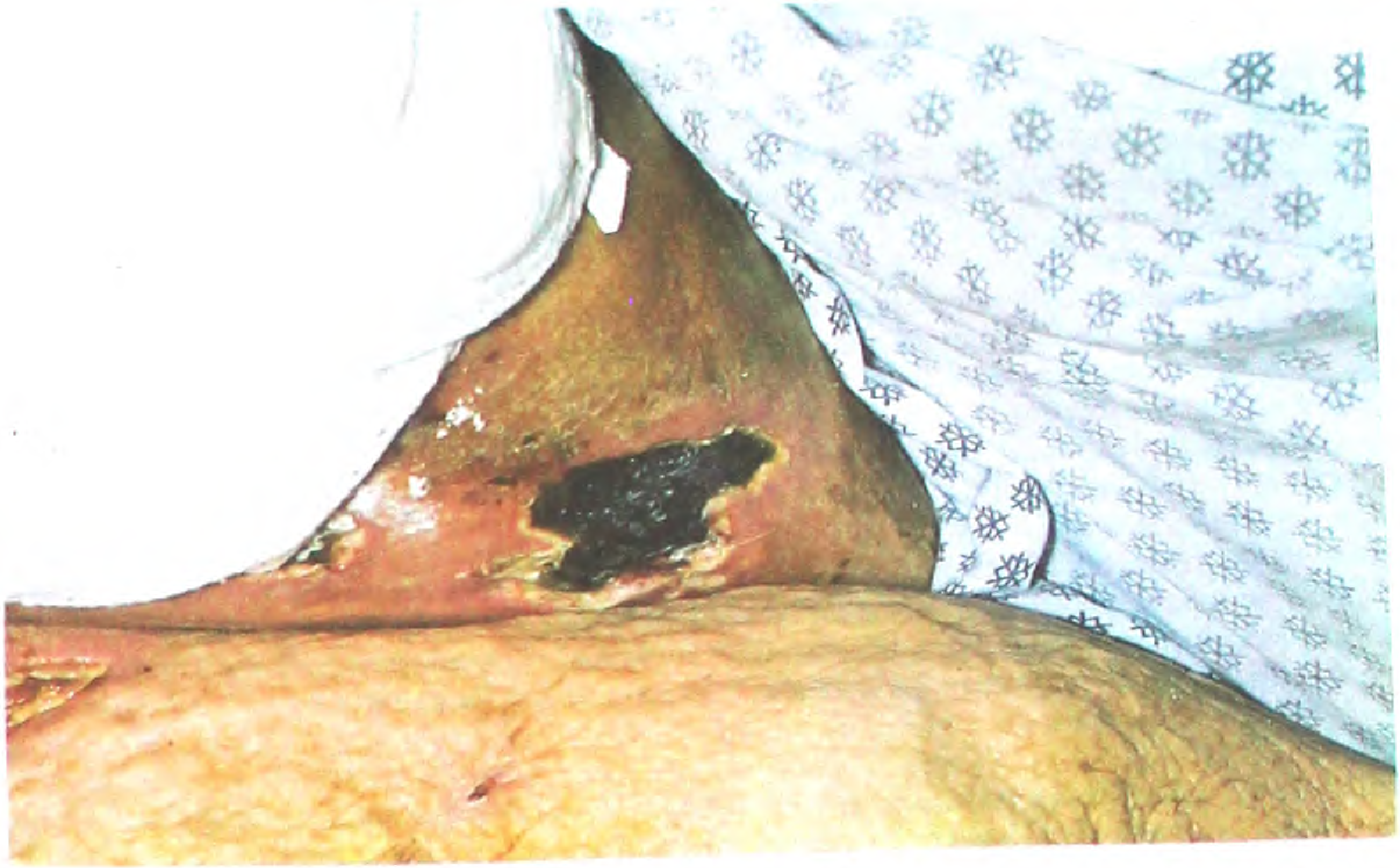
What is your Diagnosis?

Riyaz Bashir MD, Faroque A Khan MACP.



A 72 year old white female with history of hypertension, congestive heart failure, atrial fibrillation and end stage renal disease on hemodialysis presented with severe pain lower abdomen and upper thighs. On physical examination her blood pressure was 140/64 mmHg, respiratory rate was 16 breaths per minute, pulse was 82 bpm and she was afebrile. Her skin examination revealed warm, tender and erythematous lesions with occasional blisters over lower abdomen and thighs extending upto the knees on both sides. Rest of the physical examination was unremarkable except for mild to moderate bilateral pitting edema.

Laboratory work-up revealed of 10.3 mgs/dl (8.5-10.5 mgs/dl), Albumin of 2.6 gms/l (3.5-5.0 gms/l), Alkaline Phosphatase was 204 U/l (30-115 U/l), and Inorganic phosphate was 8.7 mgs/dl (2.5-4.5 mgs/dl). Parathormone levels were 112 pmoles/l (1.0-6.8 pmole/l). Patient was diagnosed to have secondary hyperparathyroidism. Her skin lesions progressively worsened and developed eschar (figure). A diagnostic skin biopsy was done.

What is your diagnosis?
(See page : 322)

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What is your Diagnosis ?

(Refer Page 321)

Diagnosis : Our patient's skim biopsy revealed vascular calcifications in the small and medium sized vessels of the skin and subcutaneous tissue, which was consistent with Calciphylaxis.

Calciphylaxis is a syndrome of disseminated calcification found in chronic renal failure patients with secondary hyperparathyrodism. This result in soft tissue calcification and vascular medial calcinosis leading to subsequent ischemic tissue necrosis. It is a rare condition in which the patient presents with painful, violaceous molted lesions of the extremities and or trunk processing to skin and subcutaneous tissue necrosis, non-healing ulcers an gangrene. The pathogenesis of this condition is not well known.

Calciphylaxis usually presents as indurated ***lesions*** most commonly seen on the thighs and abdomen and as digital gangrene. These lesions progress and get complicated with eschar formation. Pain and pruritis are the most common symptoms. Almost all of these patients have elevated PTH levels hence hyperparathyroidism should be present before entertaining this diagnosis. Tissue biopsy demonstrates vascular and soft tissue calcification.

The ***treatment*** of this syndrome is primarily supportive. This involves 1. Local wound care in the form of debridement and systemic antibiotics for infected lesions. Occasionally hyperbaric oxygen is also used. 2. Correction of electrolyte abnormalities is also very important, however $CaCO_3$ is not used as a phosphate binder since it increases the risk of hypercalcemia and calciphylaxis[1]. 3. Parathyroidectomy is definitive treatment. Usually three and a half gland parathyroidectomy with autotransplantation in the forearm is done. This has been shown to provide a dramatic improvement in the peripheral lesions.

Calciphylaxis is reported to be associated with very ***high mortality***[1] (up to 58 per cent). According to Chal et al, lesions involving the truck had a higher mortality than those on the extremities[2]. Also extensive eschar formation over the wounds was associated with poorer prognosis. The cause of death is usually uncontrollable sepsis from wound infection[3].

Our patient was initially managed with broad-spectrum antibiotics and debridement. After the diagnosis of Calciphylaxis, she underwent three and a half gland parathyroidectomy with improvement in her symptoms of pain and normalization of her electrolytes. However, due to fulminant sepsis which required vasopressors she died on the day 22 following surgery.

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VIAGRA Some Hard truths

No drug in medical history has either announced its arrival with such a bang or generated so much interest among the media, the medical profession and the lay public. Time magazine recently carried a cover story on Viagra, an honour that they generally bestow on earth-shaking events, or on men and women of extraordinary accomplishment either in their life-time or, even posthumously. Very few 'births' receive Time covers. Yet, a relatively new drug that hasn't even been time-tested and certainly cannot claim to be earth-shattering walks away with a cover. This is intriguing because impotence is not a life-threatening condition and many are even sceptical whether it even constitutes a major health problem.

What is Viagra?

Viagra is Pfizer's proprietary name for sildenafil. It was originally intended for use in patients with cardiovascular disease, an area where its usefulness turned out to be a disappointment. Patients receiving the drug reported improved erections. This prompted research on sildenafil for male erectile dysfunction (MED). The rest, as they say, is history. It was marketed as a 100 mg tablet.

How does Viagra act?

A man's ability to attain and sustain an erection is in part dependent upon the concentration in the penis of an enzyme called cyclic GMP. Cyclic GMP in the penis is normally broken down by another enzyme. called phosphodiesteras 5 (PDE 5). Sildenafil viagra breaks down PDE 5 and thus allows the man's native cyclic GMP to last longer. This, in bedroom parlance, translates into longer-lasting and harder erections.

Does Viagra help all men?

The answer is an emphatic NO. Viagra helps only about 60 per cent of men with erectile dysfunction. By comparison, nearly 30 per cent of men receiving a placebo also report improvement. This means that Viagra is only twice as effective as placebo in treating erectile dysfunction. Studies of Viagra's efficacy are not always quantified i.e. objectively measured. Much of the improvement reported in clinical studies is based on patients' subjective experience. This makes the dividing line between its pharmacological efficacy and its placebo effect rather hazy.

Sildenafil helps only those patients who have a cyclic GMP deficiency. Clinically, these are identified as patients with proven organic vasculogenic impotance. This diagnosis is established after the performance of certain special tests which can identify defects in the arteries, or veins of the penis. Only patients with mild to moderate vascular disease are likely to benefit from this drug. Thus, the elderly male with mild to moderate erectile difficulty who does not have significant diabetes or vascular disease (high blood pressure and heart problems) is the ideal candidate for sildenafil.

This means that normal men, patients with purely psychological disease, those with severe vascular insufficiency and those with non-vascular causes of impotance will not derive benefit from the drug. It is wrong to suppose that sildenafil is an aphrodisiac for all. However, if it is borne in mind that physical rather than purely psychological factors are identifiable in nearly 80 to 90 per cent of men with erectile dysfunction, it becomes clear that many stand to benefit from the drug.

How does one use Viagra?

A 100 mg tablet of Viagra (high-end dose) is taken an hour or an hour-and-a-half before anticipated sexual intercourse. Viagra does not produce erections on demand in non-sexual situations and this must be understood. It would befit physicans and patients alike to bear this in mind to avoid not only disappointment but wasteful expenditure. After all, at U.S. $ 10 per tablet (and up to Rs 1200 in the Indian grey market), the drug doesn't come cheap.

How safe is it?

Recent reports of deaths in Viagra users and its visual and other side effects have brought the wonder drug down to earth with a rude thud. Viagra is strictly contraindicated in patients receiving nitroglycerin for coronary artery disease. It should also be prescribed with prudence in many other clinical situations. History reminds us that new drugs in the market must always be approached with temperance. Just because a drug has received FDA approval, it does not make it 100 per cent safe. Many drugs have been aggressively launched in the past, and only much later that many new, previously unreported, and often dangerous side effects have come to light prompting sudden warning lables or a withdrawal altogether of the concerned drug.

Let us not forget the thalidomide tragedy. Thalidomide was a researched, tested and approved drug. One has only to have seen a picture of a phocomelic or amelic baby once to realise that man forgets the lessons that history repeatedly tries to teach him.

The Indian scenario

With a population of close to a billion, and an impotence prevalence rate of 10 per cent among the adult male population, the scope for sildenafil in the Indian market leaves little to the imagination!

The pharmaceutical industry, is on its way to launching the Indian edition of the drug soon. The good news is that the drug will be available at less than a tenth of its international price. The bad news is that prescription control in India is non-existent and sildenafil will be sold freely as an OTC (over the counter) drug. This will result in patients bypassing their physicians, with a consequent increase in side effects.

Perspective

The quest for virility-enhancing drugs is not new, in fact it is as old as mankind. This is hardly surprising because sex is man's second strongest instinct (next only to survival). Multi-billion dollar aphrodisiac industries have flourished in all civilisations. Viagra is just the pharmaceutical industry's version of the same and an attempt to hitch on to the same bandwagon. Every few years, a new oral drug comes, and, with predictable regularity, goes. The last decade has seen the rise and fall of yohimbine, trazodone, fluoxetine, phentolamine among others. It will not be surprising if sildenafil goes the same way. Indeed, its predecessors seem to have already set a repetitive and gloomy pattern. So let's not get carried away.

Side Effects of Viagra

Headaches
Visual Disturbances
-blurring of vision, seeing blue or green
-long-term effects on vision unknown

Blackouts and Dizziness
-due to sudden drop in blood pressure
-occurs especially in patients receiving nitroglycerin or medication fo high BP

Flushing
Dyspepsia
Diarrhoea
Nasal congestion
Urinary tract infections
Rash
Priapism

-a persisten,t painful erection which may sometimes require surgery for cure and which, if not treated in time, can render a man permanently impotent.

Sudden death
-in patients receiving nitroglycerin
Dependence
-its dependence-producing propensity with long term use is not yet known.

Compiled *by FA Bhat & ZA Khatib*

Notice:-

All the authors are requested to follow instructions strictly.

Please send black and white photographs.

For coloured pictures the cost has to be paid by author's in advance.

Please use minimum no. of pictures, tables and references in articles.

Clinical Skills Assessment (CSA): New Requirement for ECFMG Certification

Musarat Shareefe, M.D. Faroque A. Khan, M.B., M.A.C.P.

Effective July 1, 1998, all international medical graduates (MG's) will be required to take a clincial skills assessment (CSA) examination, in addition to USMLE Step I (Basic Sciences), USMLE Step II (Clinical Sciences), and an English language profficiency test for certification by ECFMG and, subsequently, to enter residency programs in the USA -which, incidentally, is getting more difficult with over 10,000 IMG's who remained unmatched after the 1998 NRMP results were announced in March 1998.

CSA Examination

The purpose of the CSA examination is to ensure that graduates of foreign medical schools can demonstrate the ability to gather and interpret clinical patient data, and communicate effectively in the English language at a level comparable to students graduating from US medical schools.

The CSA examination consists of 10 testing stations. In each station examinees will encounter a standardized patient (SP)— a lay person trained to accurately and consistently portray a patient. SP's will respond to questions from examinees with answers appropriate to the case and, upon physical examination, will demonstrate appropriate physical findings. Examinees will be expected to proceed through each encounter with an SP as they would with a real patient. The test cases represent the major clinical disciplines encountered at medical schools in the US and Canada — including Internal Medicine, Surgery, Ob/Gyn, Pediatrics, Psychiatry and Family Medicine. There will be a balance of genders, ages and ethnicity among SP's on any assessment.

Each of the 10 CSA encounters will allow the examinee 15 minutes to interact with the SP and following each encounter, the examinee will have 10 minutes to complete the patient note. The patient note should be similar to the medical record one would compose after seeing a patient in a clinic or emergency department. The examinee should record important medical history, physical findings, differential diagnosis and important diagnostic studies one would order next. The total administration time is approximately six hours. Ten out of eleven cases will be assessed.

Assessment

The specific skills being documented are:

a. ability to elicit an appropriate history.
b. ability to perform an accurate, focussed physical examination.
c. demonstration of interpersonal skills appropriate to a physician-patient interaction.
d. generation of a legible, organised, complete and accurately written record of the encounter.
e. proficiency in spoken English.

A report of performance on CSA will consist of a pass/fail designation. For purpose of ECFMG certification, there is no limit on the number of attempts allowed to pass the CSA examination. Scoring components consist of two parts — the first component called the integral clinical encounter (ICE) is a combination of data gathering (DG) and patient note (PN) scores. The second component, communication skills (COM), is derived from combining the SP evaluation of interpersonal skills (IPS) and spoken English proficiency (ENG).

The results of the CSA examination — an overall pass/fail designation — will be reported to the examinee six to eight weeks after adminstration of the CSA examination. This Pass ECFMG Certificate is valid for three years from the date it is issued.

Registration and Schedule

The application form (Form 706 in the pink application packet) for the CSA examination has been inserted into the 1998 ECFMG information booklet. The application form must be completed in full and sent to ECFMG, along with the current CSA registration fee of $1,200/= (U.S. dollars). At that point, notification of registration for the CSA examination will be mailed to the applicant. Once the notification of registration is received, the applicant may schedule a date to take the

JK Practitioner 1998; 5(4): 325-326

From : Nassan County Medical Centre, East-Meadows, NY Deptt. of Medicine (Prof. Khan, Shareefe For further information Farooque A. Khan MB, MACP, Chairman, Nassa County Medical Centre 2201, Hempstead East Meadow New York 11554.

CSA examination. Applicants must schedule the CSA examination within four months of, and must take the CSA examination within one year of, the date indicated on the notification of registration. failure to schedule the CSA examination within four months, or to actually take CSA within one year, will require submission of a new application and fee.

To schedule a test date, one of three ways can be utilized:

a) by writing to ECFMG.
b) by telephone-contact CSA Examination Scheduling Programe at number 1-215-790-1982 (Monday to Friday, 9899-2400 EST).
c) directly schedule your test date through Internet-ECFMG web site at http://www.ecfmg.org.

When an acceptable date is found, an admission permit confirming the date, time, and location of the assessment will be mailed to the applicant. Applicants must present this admission permit at the Clinical Skills Assessment Centre. Once a test date is scheduled, it cannot be canceled or rescheduled. The ECFMG will be able to examine up to 14,000 candidates each year.

The CSA examination will be administered throughout the year, except on major US holidays, starting July 1, 1998 at the following location:

ECFMG
3624 Mark Place
CSA Center-Third Floor
Philadelphia, PA 19104 U.S.A.

Prerequisites

Eligibility to take the CSA examination has the same requirements as required fore registering for ECFMG. In addition, the applicant should have passed the required medical science examination in the Basic Medical and Clinical Sciences tests, and the English language proficiency test. (USMLE Step I and Step II, and English language proficiency test)

Comment

This is the first time ECFMG is offering an examination only in the USA. For IMG's who are desirous of pursuing their career in the USA from those countries neighboring the US, or from European states, it may be within an aforadable travelling distance. However, for those from the Asian subcontinent and/or Far East, it may seem like a Herculean task. The process for taking the CSA examination entails the requirement of travel documents, visa and immigration issues which are likely to cause tremendous financial strain. For those with no friends or relatives in the USA, the issue of accomodations is a major hurdle, as well. There's also a possibility that an applicant may have to take the examination more than once, and there's no assurance that the second test day will fall within the same visit period.

With innumerable numbers of IMG's who are already ECFMG certified and are awaiting to join residency programs, there's no gurantee of subsequently obtaining a residency position after passing the CSA examination.

As of now, the IMG's who are ECFMG certified as of June 30, 1998 are permitted to, but not required to, take the CSA examination. However, there are indications that starting in 1999 all candidates may be required to pass this examination to enter residency programs.

The scenario for IMG's particularly those who require J-1 visas, to enter the US for pursuing their medical careers seems grim. Depending on the experience gained with this new CSA examination, it is expected that in the future some more CSA examination centers may be opened in Europe/the Middle East, etc. However, this is not likely to occur in the near future.

The purpose of this brief report is to provide prospective IMG's with the current status of the training requirements for becoming eligible for training in the USA. Even for those who become eligible, the odds of obtaining a training position are not good. We hope that the applicants consider this report seriously before embarking on a costly adventure. Forewarned is forearmed.

Helicobacter Pylori Infection in Endoscopic Biopsy Specimens of Gastric Cancer: A Preliminary Evaluation in a High Risk Population of Kashmir Valley

The aim of the present study was to assess the prevalence of Helicobacter pylori (H.pylori) infection in Kashmiri patients with gastric cancer and to compare this with a matched control population.

Fifty patients with gastric cancer and thirty age/sex matched controls were included in the study. All the subjects were hailing from Kashmir Valley. For detection of H. pylori biopsy specimens were used both from cases and controls. An insignificant association was shown between H. pylori and both intestinal and diffuse type of gastric cancer.

The data provides support against the significant association between H. pylori and gastric cancer in this part of world, a place where the age standardized incidence of gastric cancer is alarmingly high. We conclude that other factors like personal and special dietary habits of Kashmiri population may be more important for the development of gastric cancer.

Source: G.M. Malik; S.Kadla; M. Mubarik, T. Hussain, G. Jeelani, J. Basu S. Rashid M. Ahmad, A. Nafee and A.R. Khan.
Diagnostic & Therap. Endosc 1997; 4 : 35-42

Osgood-Schlatter disease

261 patients with 365 knees treated for Osgood-Schlatter disease, 237 patients responded readily to the conservative treatment, consisting of restriction of sports activity and analgesics. None of these patients treated conservatively had plaster cast immobilization. The remainder of the patients (27 knees) had an operation where the loose ossicle/ossicles were removed from the proximity of the tibial tubercle. The main indications for the operation were tender mobile loose ossicle/ ossicles/ with symptoms of pain on mild activity especially kneeling. Following the operation all patients returned to their normal activities.

Source: A. Hussain; G.A. Hagroo.

Tumoricidal activity of povidone-iodine

Local recurrence after "curative" colorectal cancer surgery has been explained by three potential mechanisms. Implantation of viable exfoliated cancer cells by the use of tumoricidal agents can be the mechanism which has failed suggest the authors from the University of Leuven, Belgium. In this study, the authors aimed to investigate the influence of bacteria, faecal matter, albumin, blood components (RBCs, plasma, haemoglobin) on the ability of povidone-iodine (in varying concentrations) to kill human colonic carcinoma cells in vitro.

Distilled water and povidone-iodine at concentrations of 0.04, 0.4, 0.8, 2 and 4% were used on human SW 620 colonic cancer cells. In the presence of the extraneous materials mentioned above, the cell MTT test.

Role of ET-I in colorectal live metastases

This is a study from the University College Medical School, London, UK. The authors report that Endothelin 1 (ET-1) which is a vasoconstrictor peptide has been implicated as a tumour growth stimulator and angiogenesis factor. The aim of this study was to assess the importance of ET-1 in colorectal cancer.

Immunoelectron microscopy for ET-1 was performed in normal liver and colorectal liver metastases. ET-1 plasma levels were measure by RIA in colorectal cancer patients with live metastases (18 patients and without metastases (12 patiets) and in the controls (22 patients). Normal patients were 6 in number.

After analysis, the authors found that in the normal liver, ET-1 was present in the endothelial cells. Whereas, in tumour, it was present in the endothelial cells, tumour cells and myofibroblasts.

The mean plasma levels, of ET-1 were 2.75 pg/ml in controls, 4.53 pg/ml in colorectal non-metastasis patients and 3.92 pg/ml in on-metastatic disease.

In conclusion, the authors feel that ET-1 may have a role in modulating tumour vascular tone. It can also modify tumour growth and angiogenesis both in a local and systemic manner. The stress that future studies may be required to indicate if increased ET-1 levels indicated disease progression.

Sources: Shankar, Loizidou, Alieve, Fredericks, Holt, Boulos, Burnstock, Taylor. "Raised endothelin-1 levels in patients with colorectal liver metastases"; British Journal of Surgery, Vol. 85, 1998; pages 502-506.

A new marker for human ductal pancreatic adenocarcinoma

Exocrine pancreatic tumours do not express sufficient amounts of somatostatin receptors unlike pancreatic neuroendocrine tumours. Hence new imaging possibilities for early diagnosis of the devastating exocrine pancreatic adenocarcinoma could be welcome. Researches from Berne, Switzerland tried to look for receptors for small regulatory peptides that may be expressed in high density and with high incidence of exocrine pancreatic adenocarcinomas.

The researchers assessed the receptors for the regulatory peptide neurotensin in vitro by receptor audiography in 24 ductal pancreatic adenocarcinomas, 20 endocrine pancreatic cancers, 18 chronic pancreatic cases and 10 normal pancreatic glands.

The results showed that some 75% of all ductal pancreatic adenocarcinomas, most of which were differentiated, were neurotensin receptor positive, whereas endocrine pancreatic cancers did not express neurotensin receptors. These receptors were not found in chronic pancreatitis or normal pancreatic tissues including pancreatic acini, ducts and islets.

The authors conclude that the selective and high expression of neurotensin receptors in ductal pancreatic adenocarcinomas could form the molecular basis for potential clinical applications, like in vivo neurotensin receptor scintigraphy for early tumour diagnosis, radiotherapy with radiolabelled neurotensin analogus and chemotherapy with neurotensin receptor antagonisis.

Source: Reubi, Waser, Friess, Buchler, Laissue. "Neurotensin receptors: a new marker for human ductal pancreatic adenocarcinoma"; GUT; Vol. 42, No. 4, April 1998; pages 546-550.

New study says ACE-Inhibitors prevent Cancer

A new study suggests ACE-inhibitors treatment may be associated with a reduced risk of developing cancer.

The possibility that ACE-inhibitors may prevent cancer has arisen after observations in animal studies that angiotensin stimulates neovascularisation (the formation of new blood vessels which tumours need to grow). In addition, ACE-inhibitors have been shown to reduce neovascularisation and tumour growth in rats.

The latest study, presented at the International Society of Hypertension meeting in Amsterdam on June 10th, is a retrospective review of data from patients treated at the Glasgow Blood Pressure Clinic in the UK. It includes 1,559 patients who received an ACE-inhibitor and 3,648 who received other blood pressure lowering medications. These patients were compared with two control populations of 2.7 million and 15,000 individuals from the same area.

Patients receiving ACE-inhibitor displayed a 28% reduced chance of developing cancer compared with the control populations (relative risk 0.92). The patients receiving other types of antihypertensive medication displayed similar risk as the control populations (relative risk 1.1).

Fatal cancers were reduced by 35% (relative risk 0.65) in the ACE-inhibitor patients, but were not reduced in the patients receiving other antihypertensives (relative risk 1.0).

The risk of cancer was reduced further in those patients taking ACE-inhibitors for more than three years. This group had a 43% reduced risk of developing cancer (relative risk 0.57).

The study also reassures on the safety of calcium blockers. It found no evidence of an increased risk of cancer with these agents (relative risk 1.0).

Speakers noted that this is a hypothesis generating study, which raises the possiblility that ACE-inhibitors protect in some way against cancer, but that it must be confirmed by randomised clinical trials.

Helicobacter pylori infection-The importance of eradication in patients with gastric disease

Discovery of Helicobacter pylori infection in patients with peptic ulcer disease has completely transformed the approach to the disease. Implications of this discovery for healthcare in general and for medical economics are only now being appreciated. Noninvasive and invasive methods of establishing the presence of information are currently available, and clinical introduction of the recently approved urea breath test in the near future will add another method for documenting both active infection and successful eradication. Patients with initial presentatioln on recurrence of gastric or duodenal ulcer disease and those with previous disease who are receiving maintenance therapy should be treated for H pylori infection. Treatment regimens, which consist of combinations of antibictics, bismuth salts, and proton pump inhibitors, can result in cure rates of 90%, with prevention of recurrence. Understanding of the infection continues to grow rapidly, and current recommendations regarding diagnosis and treatment will evolve as new methods are developed.

Source: Bonagura, A.F., Dabezies M.A. Postgrad. Med. (1996) 100, No.5, p. 115-129.

Gastrointestinal effects of NSAIDs-Difficulties in detection and management

Nonsteroidal anti-inflammatory drugs (NSAIDs) and acetylsalicylic acid are effectivo analgesic agents, but their use carries a significant potential for gastrointestinal side effects. Because many persons who have serious adverse effects from NSAIDs are asymptomatic, the decision to use these drugs must be tempered by an understanding of the side-effect profile and knowledge of who constitutes the high-risk population. Patients must be vigilantly monitored for signs and symptoms of reactions to the drugs, which should be discontinued when injury is suspected if at all possible. Diagnostic endoscopy should be the mainstay of further evaluation. Treatment of NSAID-induced gastrointestinal disease parallels that of non-NSAID-related reactions. This includes use of histamine$_2$ receptor antagonists or proton pump inhibitors. Although NSAID-induced ulcers can heal while the drugs are continued, only omeprazole (Prilosec) has been shown to speed healing during NSAID use. For persons at highest risk, consideration must be given to prophylaxis against peptic ulcer disease. Misoprostol (Cytotec) has been clearly shown to offer the best protection against gastroduodenal ulceration.

Source: Pearson, S.P., Kelberman, I. Postgrad. Med. (1996) 100, No.5, p.131-142.

Primary prophylaxis of variceal bleeding in cirrhosis: A cost-effectiveness analysis

Prophylaxis against the first variceal bleeding has been proposed to reduce morbidity and mortality in cirrhotic patients. No previous information is available regarding the cost-effectiveness of prophylaxis. The aim of this study was to compare the cost-effectiveness of variceal bleeding prophylaxis with propranolol, sclerotherapy, and shunt surgery in cirrhotic patients stratified by bleeding risk.

A hypothetical cohort was stratified according to bleeding risk. The natural history of cirrhosis with esophageal varices was simulated using a Markov model. Transitional probabilities extracted from published studies and costs were obtained from the institution's billing department. Sensitivity analysis were performed for important variables.

Propranolol results in cost savings ranging between $450 and $14,600 over a 5-year period. The extent of cost savings depended on the individual patient's bleeding risk. In addition, propranolol increased the quality-adjusted life expectancy by 0.1-0.4 years. Sclerotherapy was significantly less cost-effective than propranolol and had no advantage on quality of life. Shunt surgery was effective therapy for prevention of bleeding but decreased life expectancy and quality of life in some risk groups and was not cost-effective.

Proporanolol is the only cost-effective form of prophylactic therapy for preventing initial variceal bleeding in cirrhosis regardless of bleeding risk.

Sources: Teran, J.C., Imperiale, T.F., Mullen, K.D., Travill, A.S., McCullough, A.J. Gastroenterology (1997) 112, No. 2, p. 473-482.

Endoscopic treatment of early oesophageal or gastric cancer

Endoscopic treatment has become increasingly popular in recent years as an alternative to surgical treatment with the hope of offering superior quality of life (QOL) for the patient. The results of endoscopic treatment of mucosal lesions of mostly early oesophageal or gastric cancer performed in 145 patients (155 lesions) over the past eight years were reviewed from the standpoint of QOL.

In 56 patients who underwent radical resection of the oesophageal mucosa, no serious complications and symptoms occurred, with epithelisation completed within about a month. Patients also showed good results regarding dietary intake and performance status (PS), and all are currently alive without any sign of recurrence. One time fractionated endoscopic resection was carried out in about 40% of the 57 patients who underwent gastric mucosal resection. In these 57 patients, an artificial ulcer measuring 3 cm or more was formed, resulting in a favourable outcome after healing. An overwhelming proportion of these subjects had no symtpoms and good PS after the treatment.

The introduction of this method, endoscopic mucosal resection using a cap fitted panendoscope, is expected to permit additional indications for endoscopic treatment. Endoscopic Nd-YAG laser irradiation was applied mainly to early gastric cancer lesions (32 patients), usually for relative indications for endoscopic treatment. This procedure is safe and advantageous in that it requires no hospitalisation, permits fractionated irradiation, and secures good QOL.

Sources: Takeshita, K., Tani, M., Inoue, H., Saeki, I., Hayashi, S., Honda, T., Gut (1997) 40, No. 1, p. 123-127.

Which peptic ulcers bleed?

The incidence of ulcer bleeding has not decreased despite effective medical treatment of peptic ulcer disease. Numerous studies have been performed on risk factors for ulder bleeding, but only a few studies have related the risk of developing ulcer bleeding to the risk of developing uncomplicated ulcer disease.

This study was performed as a multicenter interdisciplinary case-control study and was based on diagnosis by endoscopy, prospective data collection, and multivariate analysis. To every patient with ulcer bleeding (case) one patient with uncomplicated peptic ulcer proven at endoscopy (control) was assigned with regard to sex, ulcer localization, and age (+5 years). The controls were randomly taken from three sources: inpatients, outpatients, and patients treated by a private physician.

Owing to strict inclusion and exclusion criteria, 209 matched pairs were available for evaluation out of 401 patients with peptic ulcer bleeding. in univariate analysis the duration of ulcer pain and the number of previous ulcer treatments proved to be protective factors for ulcer bleeding. The intake of nonsteroidal anti-inflammatory drugs (NSAID) as a whole, acetylsalicylic acid (aspirin), and paracetamol gave and increased risk for ulcer bleeding. Multivariate analysis identified four risk factors for peptic ulcer bleeding: lung disease, NSAID intake, no pretreatment with H_2 blockers, and acetylsalicylic acid intake.

The following patient groups represent a risk for peptic ulcer bleeding: multimorbid patients, receiving NSAID and/or aspirin, and patients with no previous ulcer history.

Sources: Imhof, M., Ohmann, C., Hartwig, A., Thon, K.-P., Hengels, K.-J., Roher, H.-D., Dusuk study group. Scand. J. Gastroenterol. (1997) 32, No. 2, p. 131-138.

What are Appropriate End-points for Helicobacter pylori Eradication in the Treatment of Duodenal Ulcer?

The end-point of Helicobacter pylori eradication trials in peptic ulcer disease should be the presence or absence of continuing H.pylori infection, and not ulcer healing or recurrence. This is not to suggest that ulcer healing or prevention of recurrence is not the desired clinical end-point. It is to allow large trials to be conducted in a 'patient-friendly' manner and in a shorter time-scale, both of which reduce patient withdrawals, protocol violations and cost. For the same reasons, diagnosis of cure should be made by noninvasive means whenever possible.

It is currently imposssible to make anything other than generalisations regarding the relative efficacies of modern eradication regimens. As it seems unlikely that definitive head-to head studies will be performed, the conduct and reporting of current trials needs to be improved and standardised, to allow meaningful comparisons. In particular, the course of each and every patient through the trial should be fully and clearly reported, especially withdrawals and dropouts. The primary efficacy analysis should be the intention-to-treat analysis, with per protocol and modified intention-to-treat analyses also reported, where appropriate.

Sources: Mathew P. Willams and Roy E. Pounder Drugs 1998 July 56(1) 1-10.

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Appointment *MD F.A.C.G.*
Date given on……………… *Ph. No. 32060*

Meet the Professor

Name : **Ghulam Mohammad Shah**
Address : Dr. G.M.Shah,
Bulbul Bagh, Barzulla Srinagar-19005 India Tele (Res) 0194-430106
Education : B.Sc, MBBS, MD (Physiology)

Additional Trainings:

1. Fellowship in Haematology, School of Tropical Medicine, Calcutta, India.
2. Fellowship in Neurophysiology - All India Institute of Medicine Sciences, New Delhi.
3. Fellowship Cardiovascular Physiology- State University of New York, Bufallo, N.Y., USA.
4. Certificate Course for Medical Teachers Training - PGI Chandigarh.

Professional Experience:

Director-Principal Imam Hussain (a.s.) Medical College & Hospital, Srinagar upto date.
Principal and Professor, Head of the Department of Physiology, Jhelum Valley College of Medical Sciences and Hospital Srinagar, Kashmir,India.
Professor & Head of the Department of Physiology, Govt. Medical College, Srinagar, Kashmir, India.
Associate Professor of Physiology, Govt. Medical College, Srinagar, Kashmir, India.
Assistant Professor of Physiology, Govt. Medical College, Srinagar, Kashmir, India.
Demonstrator, Department of Physiology, Govt. Medical College, Srinagar, Kashmir,India.
Medical Officer incharge of various District Hospitals and Health Centres of J&K State Health Department.

Administrative Experience:-

1. Principal, Jhelum Valley Medical College and Hospital, Srinagar, Kashmir, India.
2. Head of the Department of Physiology, Govt. Medical College, Srinagar, Kashmir, India.
3. Principal/Dean, Govt. Medical College, Srinagar Kashmir, India in the absence of the permanent Principal/Dean.
4. Administrator, Associated Hospitals of the Govt. Medical College, Sgr. Kashmir in the absence of the permanent incumbent.
5. Director Health Services Jammu & Kashmir Government.

Research and Publications:

Guided Research Programme of about one dozen Post-graduate students leading to the award of M.Sc, M.Phil , MD, Ph.D degrees both in India and Abroad. Published 20 papers both in Indian and Foreign journals.

Membership of Academic Bodies

1. Member Syndicate Kashmir University - 1 year
2. Chairman, Board of studies (Physiology), University of Kashmir for 25 years.
3. Member, Faculty of Medicine, University of Kashmir for 25 years.
4. Member Secretary of the Selection Committee for MBBS course for Government Medical College of Jammu and Kashmir.
5. Member of the Board of Post-graduate Studies.
6. Member of the Physiology Post-graduate Selection Committee for the University of Kashmir.
7. Member of the Staff Selection Commission for Physiology:
    - i) Union Public Service Commission, New Delhi India.
    - ii) Delhi University, India.
    - iii) Aligarh University, Aligarh, India.
8. Examiner in Physiology-MBBS/MD/M.Sc/M.Phil/ Ph.D, BDS and B-Pharmacy in various University of India and abroad.

Affiliation

1. Membership int he Association of Physiologists and Pharmacologists of India.
2. Executive Secretary-International Congress of Physiologists.
3. Associate Editor of the Journal of Physiology and Pharmacology for India.
4. Member Advisor Board "JK-Practitioner" the international Journal of Medical Science.

Q & A

Q1. How do you forsee the private medical education effecting the Govt. sector?

A. The fact that more and more doctors in Government

Sector are opting for private practice cannot be overlooked. In fact most academically dedicated teachers in all Medical Colleges and even in priemere Institutions of the Country are lea ving their jobs and taking up private practice. The result is that full time, qualified, experienced teachers who fulfill the criteria of Medical Council of India for appointments as faculty staff in Medical Colleges are are becoming increasingly non-available. Thus it is necessary for Medical Council of India to change its rules for academic appointments and go back to the past for filling up teaching posts by permitting well qualified experienced doctors in various specialities to be appointed on honorary/part-time teachers in the Medical Institutions so that the Medical Education does not suffer. This hasbecome necessary as more and more Medical College are being established both in Government and Private Sector. It will also benefit such teachers by continuous Medical Education.

Q2. What are you views about private hospitals coming up all over the country?

A. No Government especially of over-populated Countries like ours can afford provviding health care to the general public free of charge. In order to provide good and efficient health care for all, it is necessary that private sector shoulod be encouraged to take up this responsibility. Already, in whole of the country, an increasingly large number of hospitals are coming up in private sector. However, it is the responsibility of the Government to have effective qualitative control over such Institutions and enforce professional standards so that the comon people are not exploited for commercial gains in the garb of publich service. One obvious advantage of such Institutions is that these will, y and large, cater forthe affluent sections of the society thus decreasing the work load on Government Hospitals. The latter will, therefore be able to rendermore effective professional service to less affluent sections of society.

Q3. What about private medical colleges?

A. With regard to the establishment of private Medical Institutions it is necessary that both State and Central Governments and affiliating Universities exerciese greater control over such institutions and give permission only when all criteria are fulfilled as per the requirements of various Statutory Bodies so that innocent students do not suffer. Otherwise such students cannot appear in any professional examination for periods of whole training course, or even more. This is not only a crime but also a sin. There is great urgency to put a stop to this kind of exploitation. It is the duty of the Government to educate public and enthusiastic parents both through print and electronic media not to admit their children in such un-authorised Medical Institutions.

Q4. Do you favour a chnage in the present medical education and examination system?

A. The time has come to drastically change the system of imparting medical education and Examination. Besides changes in curicullum it is necessary to develop a system of both horizantal and vertical integeration in teaching medical sciences and remove the present tight compartmentalization. During the training course, project work should be assigned to all students preferably in rural setting. The internees should be posted in village dispensaries to expose them to the health problems of he rural masses.

This is also high time to change the system of examination by making it more objective rather than subjective. The postgraduate Medical education also needs reform. it is not necessary to pass examination for superspecialization like DM, Ph.D etc. The postgraduates should be given more effective practical training in the basic specialization not only in their own ulmatuater but also in specialized Institutes of the country abroad.

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Musarat Shareefe, M.D. Faroque A. Khan, M.B., M.A.C.P.

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b. ability to perform an accurate, focussed physical examination.

c. demonstration of interpersonal skills appropriate to a physician-patient interaction.

d. generation of a legible, organised, complete and accurately written record of the encounter.

e. proficiency in spoken English.

A report of performance on CSA will consist of a pass/fail designation. For purpose of ECFMG certification, there is no limit on the number of attempts allowed to pass the CSA examination. Scoring components consist of two parts — the first component called the integral clinical encounter (ICE) is a combination of data gathering (DG) and patient note (PN) scores. The second component, communication skills (COM), is derived from combining the SP evaluation of interpersonal skills (IPS) and spoken English proficiency (ENG).

The results of the CSA examination — an overall pass/fail designation — will be reported to the examinee six to eight weeks after adminstration of the CSA examination. This Pass ECFMG Certificate is valid for three years from the date it is issued.

Registration and Schedule

The application form (Form 706 in the pink application packet) for the CSA examination has been inserted into the 1998 ECFMG information booklet. The application form must be completed in full and sent to ECFMG, along with the current CSA registration fee of $1,200/= (U.S. dollars). At that point, notification of registration for the CSA examination will be mailed to the applicant. Once the notification of registration is received, the applicant may schedule a date to take the

JK Practitioner 1998; 5(4): 325-326

From : Nassan County Medical Centre, East-Meadows, NY Deptt. of Medicine (Prof. Khan, Shareefe For further information Farooque A. Khan MB, MACP, Chairman, Nassa County Medical Centre 2201, Hempstead East Meadow New York 11554.

CSA examination. Applicants must schedule the CSA examination within four months of, and must take the CSA examination within one year of, the date indicated on the notification of registration. failure to schedule the CSA examination within four months, or to actually take CSA within one year, will require submission of a new application and fee.

To schedule a test date, one of three ways can be utilized:

a) by writing to ECFMG.

b) by telephone-contact CSA Examination Scheduling Programe at number 1-215-790-1982 (Monday to Friday, 9899-2400 EST).

c) directly schedule your test date through Internet-ECFMG web site at http://www.ecfmg.org.

When an acceptable date is found, an admission permit confirming the date, time, and location of the assessment will be mailed to the applicant. Applicants must present this admission permit at the Clinical Skills Assessment Centre. Once a test date is scheduled, it cannot be canceled or rescheduled. The ECFMG will be able to examine up to 14,000 candidates each year.

The CSA examination will be administered throughout the year, except on major US holidays, starting July 1, 1998 at the following location:

ECFMG
3624 Mark Place
CSA Center-Third Floor
Philadelphia, PA 19104 U.S.A.

Prerequisites

Eligibility to take the CSA examination has the same requirements as required fore registering for ECFMG. In addition, the applicant should have passed the required medical science examination in the Basic Medical and Clinical Sciences tests, and the English language proficiency test. (USMLE Step I and Step II, and English language proficiency test)

Comment

This is the first time ECFMG is offering an examination only in the USA. For IMG's who are desirous of pursuing their career in the USA from those countries neighboring the US, or from European states, it may be within an afforadable travelling distance. However, for those from the Asian subcontinent and/or Far East, it may seem like a Herculean task. The process for taking the CSA examination entails the requirement of travel documents, visa and immigration issues which are likely to cause tremendous financial strain. For those with no friends or relatives in the USA, the issue of accomodations is a major hurdle, as well. There's also a possibility that an applicant may have to take the examination more than once, and there's no assurance that the second test day will fall within the same visit period.

With innumerable numbers of IMG's who are already ECFMG certified and are awaiting to join residency programs, there's no gurantee of subsequently obtaining a residency position after passing the CSA examination.

As of now, the IMG's who are ECFMG certified as of June 30, 1998 are permitted to, but not required to, take the CSA examination. However, there are indications that starting in 1999 all candidates may be required to pass this examination to enter residency programs.

The scenario for IMG's particularly those who require J-1 visas, to enter the US for pursuing their medical careers seems grim. Depending on the experience gained with this new CSA examination, it is expected that in the future some more CSA examination centers may be opened in Europe/the Middle East, etc. However, this is not likely to occur in the near future.

The purpose of this brief report is to provide prospective IMG's with the current status of the training requirements for becoming eligible for training in the USA. Even for those who become eligible, the odds of obtaining a training position are not good. We hope that the applicants consider this report seriously before embarking on a costly adventure. Forewarned is forearmed.

Helicobacter Pylori Infection in Endoscopic Biopsy Specimens of Gastric Cancer: A Preliminary Evaluation in a High Risk Population of Kashmir Valley

The aim of the present study was to assess the prevalence of Helicobacter pylori (H.pylori) infection in Kashmiri patients with gastric cancer and to compare this with a matched control population.

Fifty patients with gastric cancer and thirty age/sex matched controls were included in the study. All the subjects were hailing from Kashmir Valley. For detection of H. pylori biopsy specimens were used both from cases and controls. An insignificant association was shown between H. pylori and both intestinal and diffuse type of gastric cancer.

The data provides support against the significant association between H. pylori and gastric cancer in this part of world, a place where the age standardized incidence of gastric cancer is alarmingly high. We conclude that other factors like personal and special dietary habits of Kashmiri population may be more important for the development of gastric cancer.

Source: G.M. Malik; S.Kadla; M. Mubarik, T. Hussain, G. Jeelani, J. Basu S. Rashid M. Ahmad, A. Nafee and A.R. Khan.
Diagnostic & Therup. Endosc. 1997; 4 : 35-42

Osgood-Schlatter disease

261 patients with 365 knees treated for Osgood-Schlatter disease, 237 patients responded readily to the conservative treatment, consisting of restriction of sports activity and analgesics. None of these patients treated conservatively had plaster cast immobilization. The remainder of the patients (27 knees) had an operation where the loose ossicle/ossicles were removed from the proximity of the tibial tubercle. The main indications for the operation were tender mobile loose ossicle/ ossicles/ with symptoms of pain on mild activity especially kneeling. Following the operation all patients returned to their normal activities.

Source: A. Hussain; G.A. Hagroo.

Tumoricidal activity of povidone-iodine

Local recurrence after "curative" colorectal cancer surgery has been explained by three potential mechanisms. Implantation of viable exfoliated cancer cells by the use of tumoricidal agents can be the mechanism which has failed suggest the authors from the University of Leuven, Belgium. In this study, the authors aimed to investigate the influence of bacteria, faecal matter, albumin, blood components (RBCs, plasma, haemoglobin) on the ability of povidone-iodine (in varying concentrations) to kill human colonic carcinoma cells in vitro.

Distilled water and povidone-iodine at concentrations of 0.04, 0.4, 0.8, 2 and 4% were used on human SW 620 colonic cancer cells. In the presence of the extraneous materials mentioned above, the cell MTT test.

Role of ET-I in colorectal live metastases

This is a study from the University College Medical School, London, UK. The authors report that Endothelin 1 (ET-1) which is a vasoconstrictor peptide has been implicated as a tumour growth stimulator and angiogenesis factor. The aim of this study was to assess the importance of ET-1 in colorectal cancer.

Immunoelectron microscopy for ET-1 was performed in normal liver and colorectal liver metastases. ET-1 plasma levels were measure by RIA in colorectal cancer patients with live metastases (18 patients and without metastases (12 patiets) and in the controls (22 patients). Normal patients were 6 in number.

After analysis, the authors found that in the normal liver, ET-1 was present in the endothelial cells. Whereas, in tumour, it was present in the endothelial cells, tumour cells and myofibroblasts.

The mean plasma levels, of ET-1 were 2.75 pg/ml in controls, 4.53 pg/ml in colorectal non-metastasis patients and 3.92 pg/ml in on-metastatic disease.

In conclusion, the authors feel that ET-1 may have a role in modulating tumour vascular tone. It can also modify tumour growth and angiogenesis both in a local and systemic manner. The stress that future studies may be required to indicate if increased ET-1 levels indicated disease progression.

Sources: Shankar, Loizidou, Alieve, Fredericks, Holt, Boulos, Burnstock, Taylor. "Raised endothelin-1 levels in patients with colorectal liver metastases"; British Journal of Surgery, Vol. 85, 1998; pages 502-506.

A new marker for human ductal pancreatic adenocarcinoma

Exocrine pancreatic tumours do not express sufficient amounts of somatostatin receptors unlike pancreatic neuroendocrine tumours. Hence new imaging possibilities for early diagnosis of the devastating exocrine pancreatic adenocarcinoma could be welcome. Researches from Berne, Switzerland tried to look for receptors for small regulatory peptides that may be expressed in high density and with high incidence of exocrine pancreatic adenocarcinomas.

The researchers assessed the receptors for the regulatory peptide neurotensin in vitro by receptor audiography in 24 ductal pancreatic adenocarcinomas, 20 endocrine pancreatic cancers, 18 chronic pancreatic cases and 10 normal pancreatic glands.

The results showed that some 75% of all ductal pancreatic adenocarcinomas, most of which were differentiated, were neurotensin receptor positive, whereas endocrine pancreatic cancers did not express neurotensin receptors. These receptors were not found in chronic pancreatitis or normal pancreatic tissues including pancreatic acini, ducts and islets.

The authors conclude that the selective and high expression of neurotensin receptors in ductal pancreatic adenocarcinomas could form the molecular basis for potential clinical applications, like in vivo neurotensin receptor scintigraphy for early tumour diagnosis, radiotherapy with radiolabelled neurotensin analogus and chemotherapy with neurotensin receptor antagonisis.

Source: Reubi, Waser, Friess, Buchler, Laissue. "Neurotensin receptors: a new marker for human ductal pancreatic adenocarcinoma"; GUT; Vol. 42, No. 4, April 1998; pages 546-550.

New study says ACE-Inhibitors prevent Cancer

A new study suggests ACE-inhibitors treatment may be associated with a reduced risk of developing cancer.

The possibility that ACE-inhibitors may prevent cancer has arisen after observations in animal studies that angiotensin stimulates neovascularisation (the formation of new blood vessels which tumours need to grow). In addition, ACE-inhibitors have been shown to reduce neovascularisation and tumour growth in rats.

The latest study, presented at the International Society of Hypertension meeting in Amsterdam on June 10th, is a retrospective review of data from patients treated at the Glasgow Blood Pressure Clinic in the UK. It includes 1,559 patients who received an ACE-inhibitor and 3,648 who received other blood pressure lowering medications. These patients were compared with two control populations of 2.7 million and 15,000 individuals from the same area.

Patients receiving ACE-inhibitor displayed a 28% reduced chance of developing cancer compared with the control populations (relative risk 0.92). The patients receiving other types of antihypertensive medication displayed similar risk as the control populations (relative risk 1.1).

Fatal cancers were reduced by 35% (relative risk 0.65) in the ACE-inhibitor patients, but were not reduced in the patients receiving other antihypertensives (relative risk 1.0).

The risk of cancer was reduced further in those patients taking ACE-inhibitors for more than three years. This group had a 43% reduced risk of developing cancer (relative risk 0.57).

The study also reassures on the safety of calcium blockers. It found no evidence of an increased risk of cancer with these agents (relative risk 1.0).

Speakers noted that this is a hypothesis generating study, which raises the possiblility that ACE-inhibitors protect in some way against cancer, but that it must be confirmed by randomised clinical trials.

Helicobacter pylori infection-The importance of eradication in patients with gastric disease

Discovery of Helicobacter pylori infection in patients with peptic ulcer disease has completely transformed the approach to the disease. Implications of this discovery for healthcare in general and for medical economics are only now being appreciated. Noninvasive and invasive methods of establishing the presence of information are currently available, and clinical introduction of the recently approved urea breath test in the near future will add another method for documenting both active infection and successful eradication. Patients with initial presentatioln on recurrence of gastric or duodenal ulcer disease and those with previous disease who are receiving maintenance therapy should be treated for H pylori infection. Treatment regimens, which consist of combinations of antibiotics, bismuth salts, and proton pump inhibitors, can result in cure rates of 90%, with prevention of recurrence. Understanding of the infection continues to grow rapidly, and current recommendations regarding diagnosis and treatment will evolve as new methods are developed.

Source: Bonagura, A.F., Dabezies M.A. Postgrad. Med. (1996) 100, No.5, p. 115-129.

Gastrointestinal effects of NSAIDs-Difficulties in detection and management

Nonsteroidal anti-inflammatory drugs (NSAIDs) and acetylsalicylic acid are effective analgesic agents, but their use carries a significant potential for gastrointestinal side effects. Because many persons who have serious adverse effects from NSAIDs are asymptomatic, the decision to use these drugs must be tempered by an understanding of the side-effect profile and knowledge of who constitutes the high-risk population. Patients must be vigilantly monitored for signs and symptoms of reactions to the drugs, which should be discontinued when injury is suspected if at all possible. Diagnostic endoscopy should be the mainstay of further evaluation. Treatment of NSAID-induced gastrointestinal disease parallels that of non-NSAID-related reactions. This includes use of histamine$_2$ receptor antagonists or proton pump inhibitors. Although NSAID-induced ulcers can heal while the drugs are continued, only omeprazole (Prilosec) has been shown to speed healing during NSAID use. For persons at highest risk, consideration must be given to prophylaxis against peptic ulcer disease. Misoprostol (Cytotec) has been clearly shown to offer the best protection against gastroduodenal ulceration.

Source: Pearson, S.P., Kelberman, I. Postgrad. Med. (1996) 100, No.5, p.131-142.

Primary prophylaxis of variceal bleeding in cirrhosis: A cost-effectiveness analysis

Prophylaxis against the first variceal bleeding has been proposed to reduce morbidity and mortality in cirrhotic patients. No previous information is available regarding the cost-effectiveness of prophylaxis. The aim of this study was to compare the cost-effectiveness of variceal bleeding prophylaxis with propranolol, sclerotherapy, and shunt surgery in cirrhotic patients stratified by bleeding risk.

A hypothetical cohort was stratified according to bleeding risk. The natural history of cirrhosis with esophageal varices was simulated using a Markov model. Transitional probabilities extracted from published studies and costs were obtained from the institution's billing department. Sensitivity analysis were performed for important variables.

Propranolol results in cost savings ranging between $450 and $14,600 over a 5-year period. The extent of cost savings depended on the individual patient's bleeding risk. In addition, propranolol increased the quality-adjusted life expectancy by 0.1-0.4 years. Sclerotherapy was significantly less cost-effective than propranolol and had no advantage on quality of life. Shunt surgery was effective therapy for prevention of bleeding but decreased life expectancy and quality of life in some risk groups and was not cost-effective.

Proporanolol is the only cost-effective form of prophylactic therapy for preventing initial variceal bleeding in cirrhosis regardless of bleeding risk.

Sources:Teran, J.C., Imperiale, T.F., Mullen, K.D., Travill, A.S., McCullough, A.J. Gastroenterology (1997) 112, No. 2, p. 473–482.

Endoscopic treatment of early oesophageal or gastric cancer

Endoscopic treatment has become increasingly popular in recent years as an alternative to surgical treatment with the hope of offering superior quality of life (QOL) for the patient. The results of endoscopic treatment of mucosal lesions of mostly early oesophageal or gastric cancer performed in 145 patients (155 lesions) over the past eight years were reviewed from the standpoint of QOL.

In 56 patients who underwent radical resection of the oesophageal mucosa, no serious complications and symptoms occurred, with epithelisation completed within about a month. Patients also showed good results regarding dietary intake and performance status (PS), and all are currently alive without any sign of recurrence. One time fractionated endoscopic resection was carried out in about 40% of the 57 patients who underwent gastric mucosal resection. In these 57 patients, an artificial ulcer measuring 3 cm or more was formed, resulting in a favourable outcome after healing. An overwhelming proportion of these subjects had no symtpoms and good PS after the treatment.

The introduction of this method, endoscopic mucosal resection using a cap fitted panendoscope, is expected to permit additional indications for endoscopic treatment. Endoscopic Nd-YAG laser irradiation was applied mainly to early gastric cancer lesions (32 patients), usually for relative indications for endoscopic treatment. This procedure is safe and advantageous in that it requires no hospitalisation, permits fractionated irradiation, and secures good QOL.

Sources: Takeshita, K., Tani, M., Inoue, H., Saeki, I., Hayashi, S., Honda, T., Gut (1997) 40, No. 1, p. 123-127.

Which peptic ulcers bleed?

The incidence of ulcer bleeding has not decreased despite effective medical treatment of peptic ulcer disease. Numerous studies have been performed on risk factors for ulder bleeding, but only a few studies have related the risk of developing ulcer bleeding to the risk of developing uncomplicated ulcer disease.

This study was performed as a multicenter interdisciplinary case-control study and was based on diagnosis by endoscopy, prospective data collection, and multivariate analysis. To every patient with ulcer bleeding (case) one patient with uncomplicated peptic ulcer proven at endoscopy (control) was assigned with regard to sex, ulcer localization, and age (+5 years). The controls were randomly taken from three sources: inpatients, outpatients, and patients treated by a private physician.

Owing to strict inclusion and exclusion criteria, 209 matched pairs were available for evaluation out of 401 patients with peptic ulcer bleeding. in univariate analysis the duration of ulcer pain and the number of previous ulcer treatments proved to be protective factors for ulcer bleeding. The intake of nonsteroidal anti-inflammatory drugs (NSAID) as a whole, acetylsalicylic acid (aspirin), and paracetamol gave and increased risk for ulcer bleeding. Multivariate analysis identified four risk factors for peptic ulcer bleeding: lung disease, NSAID intake, no pretreatment with H_2 blockers, and acetylsalicylic acid intake.

The following patient groups represent a risk for peptic ulcer bleeding: multimorbid patients, receiving NSAID and/or aspirin, and patients with no previous ulcer history.

Sources: Imhof, M., Ohmann, C., Hartwig, A., Thon, K.-P., Hengels, K.-J., Roher, H.-D., Dusuk study group. Scand. J. Gastroenterol. (1997) 32, No. 2, p. 131-138.

What are Appropriate End-points for Helicobacter pylori Eradication in the Treatment of Duodenal Ulcer?

The end-point of Helicobacter pylori eradication trials in peptic ulcer disease should be the presence or absence of continuing H.pylori infection, and not ulcer healing or recurrence. This is not to suggest that ulcer healing or prevention of recurrence is not the desired clinical end-point. It is to allow large trials to be conducted in a 'patient-friendly' manner and in a shorter time-scale, both of which reduce patient withdrawals, protocol violations and cost. For the same reasons, diagnosis of cure should be made by noninvasive means whenever possible.

It is currently impposssible to make anything other than generalisations regarding the relative efficacies of modern eradication regimens. As it seems unlikely that definitive head-to head studies will be performed, the conduct and reporting of current trials needs to be improved and standardised, to allow meaningful comparisons. In particular, the course of each and every patient through the trial should be fully and clearly reported, especially withdrawals and dropouts. The primary efficacy analysis should be the intention-to-treat analysis, with per protocol and modified intention-to-treat analyses also reported, where appropriate.

Sources: Mathew P. Willams and Roy E. Pounder Drugs 1998 July 56(1) 1-10.

DR. MALIK'S
MODERN GIT ENDOSCOPY CENTRE
Jehlum Market, Opposite General
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Refered by *Dr. G. M. Malik*
Appointment *MD F.A.C.G.*
Date given on............ *Ph. No. 32060*

Meet the Professor

Name : **Ghulam Mohammad Shah**
Address : Dr. G.M.Shah,
Bulbul Bagh, Barzulla Srinagar-19005 India Tele (Res) 0194-430106
Education : B.Sc, MBBS, MD (Physiology)

Additional Trainings:

1. Fellowship in Haematology, School of Tropical Medicine, Calcutta, India.
2. Fellowship in Neurophysiology - All India Institute of Medicine Sciences, New Delhi.
3. Fellowship Cardiovascular Physiology- State University of New York, Bufallo, N.Y., USA.
4. Certificate Course for Medical Teachers Training - PGI Chandigarh.

Professional Experience:

Director-Principal Imam Hussain (a.s.) Medical College & Hospital, Srinagar upto date.
Principal and Professor, Head of the Department of Physiology, Jhelum Valley College of Medical Sciences and Hospital Srinagar, Kashmir,India.
Professor & Head of the Department of Physiology, Govt. Medical College, Srinagar, Kashmir, India.
Associate Professor of Physiology, Govt. Medical College, Srinagar, Kashmir, India.
Assistant Professor of Physiology, Govt. Medical College, Srinagar, Kashmir, India.
Demonstrator, Department of Physiology, Govt. Medical College, Srinagar, Kashmir,India.
Medical Officer incharge of various District Hospitals and Health Centres of J&K State Health Department.

Administrative Experience:-

1. Principal, Jhelum Valley Medical College and Hospital, Srinagar, Kashmir, India.
2. Head of the Department of Physiology, Govt. Medical College, Srinagar, Kashmir, India.
3. Principal/Dean, Govt. Medical College, Srinagar Kashmir, India in the absence of the permanent Principal/Dean.
4. Administrator, Associated Hospitals of the Govt. Medical College, Sgr. Kashmir in the absence of the permanent incumbent.
5. Director Health Services Jammu & Kashmir Government.

Research and Publications:

Guided Research Programme of about one dozen Post-graduate students leading to the award of M.Sc, M.Phil , MD, Ph.D degrees both in India and Abroad. Published 20 papers both in Indian and Foreign journals.

Membership of Academic Bodies

1. Member Syndicate Kashmir University - 1 year
2. Chairman, Board of studies (Physiology), University of Kashmir for 25 years.
3. Member, Faculty of Medicine, University of Kashmir for 25 years.
4. Member Secretary of the Selection Committee for MBBS course for Government Medical College of Jammu and Kashmir.
5. Member of the Board of Post-graduate Studies.
6. Member of the Physiology Post-graduate Selection Committee for the University of Kashmir.
7. Member of the Staff Selection Commission for Physiology:
    i) Union Public Service Commission, New Delhi India.
    ii) Delhi University, India.
    iii) Aligarh University, Aligarh, India.
8. Examiner in Physiology-MBBS/MD/M.Sc/M.Phil/Ph.D, BDS and B-Pharmacy in various University of India and abroad.

Affiliation

1. Membership int he Association of Physiologists and Pharmacologists of India.
2. Executive Secretary-International Congress of Physiologists.
3. Associate Editor of the Journal of Physiology and Pharmacology for India.
4. Member Advisor Board "JK-Practitioner" the international Journal of Medical Science.

Q & A

Q1. How do you forsee the private medical education effecting the Govt. sector?

A. The fact that more and more doctors in Government

Sector are opting for private practice cannot be overlooked. In fact most academically dedicated teachers in all Medical Colleges and even in priemere Institutions of the Country are lea ving their jobs and taking up private practice. The result is that full time, qualified, experienced teachers who fulfill the criteria of Medical Council of India for appointments as faculty staff in Medical Colleges are are becoming increasingly non-available. Thus it is necessary for Medical Council of India to change its rules for academic appointments and go back to the past for filling up teaching posts by permitting well qualified experienced doctors in various specialities to be appointed on honorary/part-time teachers in the Medical Institutions so that the Medical Education does not suffer. This hasbecome necessary as more and more Medical College are being established both in Government and Private Sector. It will also benefit such teachers by continuous Medical Education.

Q2. What are you views about private hospitals coming up all over the country?

A. No Government especially of over-populated Countries like ours can afford provviding health care to the general public free of charge. In order to provide good and efficient health care for all, it is necessary that private sector shoulod be encouraged to take up this responsibility. Already, in whole of the country, an increasingly large number of hospitals are coming up in private sector. However, it is the responsibility of the Government to have effective qualitative control over such Institutions and enforce professional standards so that the comon people are not exploited for commercial gains in the garb of publich service. One obvious advantage of such Institutions is that these will, y and large, cater forthe affluent sections of the society thus decreasing the work load on Government Hospitals. The latter will, therefore be able to rendermore effective professional service to less affluent sections of society.

Q3. What about private medical colleges?

A. With regard to the establishment of private Medical Institutions it is necessary that both State and Central Governments and affiliating Universities exerciese greater control over such institutions and give permission only when all criteria are fulfilled as per the requirements of various Statutory Bodies so that innocent students do not suffer. Otherwise such students cannot appear in any professional examination for periods of whole training course, or even more. This is not only a crime but also a sin. There is great urgency to put a stop to this kind of exploitation. It is the duty of the Government to educate public and enthusiastic parents both through print and electronic media not to admit their children in such un-authorised Medical Institutions.

Q4. Do you favour a chnage in the present medical education and examination system?

A. The time has come to drastically change the system of imparting medical education and Examination. Besides changes in curicullum it is necessary to develop a system of both horizantal and vertical integeration in teaching medical sciences and remove the present tight compartmentalization. During the training course, project work should be assigned to all students preferably in rural setting. The internees should be posted in village dispensaries to expose them to the health problems of he rural masses.

This is also high time to change the system of examination by making it more objective rather than subjective. The postgraduate Medical education also needs reform. it is not necessary to pass examination for superspecialization like DM, Ph.D etc. The postgraduates should be given more effective practical training in the basic specialization not only in their own ulmatuater but also in specialized Institutes of the country abroad.

PHOTO FEATURE

DOCTOR'S DAY ORGANISED BY INDIAN MEDICAL ASSOCIATION OF INDIA (IMA), KASHMIR BRANCH, AT SKIMS, SRINAGAR ON IST JULY 1998

Inaugural Function

INDIAN MEDICAL ASSOCIATION
WELCOME YOU FOR
DOCTORS DAY CELEBRATION
ON JULY 1ST 1998
Listril

On the Stage (L to R) Prof. Mehraj-u-Din (Director SKIMS) Dr. G.M. Malik *(President IMA Kmr. Branch)* Dr. A.M. Matoo *(V.C. SKIMS)* Prof. Bhan *(Chief Guest)* Prof Z. Jeelani *(Dean SKIMS)* Prof. Ahad *(Ex-President IMA)* Dr. Mir Nazir *(Secy. IMA)* Prof. Imtiaz Ali *(Organising Secy.)*.

AUDIENCE VIEW

(a) Faculty member of SKIMS, GMC, JVC, Srinagar
(B) Ex-Professors, Ex-Directors/Dy. Directors of Health Services / IMA Members

Dr. B.C. Roy Awards of 1998

Prof. B.M. Bhan (Ex-HOD Surgery, GMC, Srinagar) receives award from Dr. M.A. Mattoo (VC SKIMS) for his excellent services both in Govt. as well as in private sector. He continued to serve his patients and people during turmoil also. He loves his native land and people (time has proved it)

Dr. M.Z. Draboo (Ex-Director Health Services) receives award from Dr. M.A. Mattoo (VC SKIMS) for his excellent services as Director, clinician and Ex-Medical Supdt. of SMHS Hospital, Srinagar

Tree Plantation in SKIMS Gardens

Prof. Allaqaband, Ex-Principal/Dean G.M.C., Srinagar

Prof. S.Z. Ahmad Ex-Director, SKIMS

Prof. Mehraj-d-Din, Director, SKIMS

A.M. Matoo V.C. SKIMS